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PART V

ENVIRONMENTAL PROTECTION AGENCY

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WATER QUALITY CRITERIA

Request for Comments

[6560-01-M]

ENVIRONMENTAL PROTECTION AGENCY

[FRL 1062-5]

WATER QUALITY CRITERIA

Request for Comments

AGENCY: Environmental Protection Agency.

ACTION: Notice.

SUMMARY: EPA is announcing the availability for public comment of water quality criteria for 27 of the 65 pollutants listed as toxic under the Clean Water Act (CWA). When published in final form after public comment, these water quality criteria may form the basis for enforceable standards. The criteria were developed pursuant to section 304 of the CWA and in compliance with a court order.

DATES: Written comments should be submitted to the person listed directly below by May 14, 1979.

FOR FURTHER INFORMATION CONTACT

Kenneth M. Mackenthun, Director, Criteria and Standards Division (WH-585), Office of Water Planning and Standards, U.S. Environmental Protection Agency, 401 M Street, SW., Washington, D.C. 20460, telephone 202/755-0100.

SUPPLEMENTARY INFORMATION:

Background

Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation.

Under paragraph 11 of the Consent Decree in *Natural Resources Defense Council, et al., v. Train,* 8 ERC 2120 (D.D.C. 1976), EPA must publish criteria for 65 specified toxic pollutants. The criteria are to state maximum recommended concentrations consistent with the protection of aquatic life and human health.

The criteria issued for public comment today are for 27 of those 65 pollutants. Criteria for the remaining 38 of the pollutants will be issued for public comment in the near future. Final publication is planned for the latter part of this year.

A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility. A criterion based on the protection and propagation of fish, shellfish and wildlife, for example, is simply the best estimate informed scientists are able to make of the maximum concentration of a given pollutant that can be tolerated while still maintaining protection of aquatic life. A criterion intended for the protection of human health, by the same reasoning, is the best estimate of the concentration which may exist and still not pose an undue risk to humans who drink water without further treatment or eat fish or shellfish from the water.

The information and scientific judgments contained in a section 304(a) criteria document could be used to develop enforceable standards under several sections of the Act such as section 302 (water quality-based-effluent limitations), section 303 (water quality standards), and section 307(a) (toxic pollutant effluent standards). It is important to observe, however, that before an enforceable standard is set under any of these statutory authorities, administrative rulemaking procedures by either the States or EPA will provide interested parties the opportunity to participate in the setting of standards. Final publication of these criteria under section 304(a) will therefore have no regulatory impact on any party.

Relationship to Water Quality Standards

Because EPA has raised significant issues about the relationship of section 304(a) criteria to section 303 water quality standards in an Advance Notice of Proposed Rulemaking ("ANPRM") (43 FR 29588, July 10, 1978), it is appropriate to highlight certain aspects of this relationship.

A water quality standard is developed through State or Federal rulemaking procedures and may be directly translated into an enforceable discharge or effluent limitation in a point source discharge (NPDES) permit under section 301(b)(1)(C), or form the basis of best management practices for nonpoint sources under section 208 of the Act. A water quality standard for a particular water body consists basically of two parts: (1) A "use" for which the water body is to be protected or "designated" (such as "agriculture", "recreation", or "fish and wildlife") and (2) a numerical or qualitative pollutant concentration limit which will support that use. (See ANPRM, 43 FR at 29589, 29590).

Establishing the use component of a water quality standard for a given water body, in light of the goals of the Act and the value of the water body for various purposes, involves a determination of what use is attainable. In determining whether a use is attainable, consideration is given to environmental, technological, social, economic and institutional factors (40 CFR 130.17(c)(1)).

The second (concentration) component of a standard, in contrast, involves a decision about the water quality or constituent concentration that must be provided if a particular use is to be maintained. Thus this component of a water quality standard, like a section 304(a) criterion, is founded on scientific considerations.

A section 304(a) criterion is not a water quality standard and in itself has no regulatory effect. Only if a section 304(a) criterion is adopted by a State through rulemaking or promulgated by EPA under section 303 (or is incorporated in a standard under another statutory authority) through rulemaking or adjudication, does the section 304(a) criterion acquire regulatory significance. Moreover, that significance is restricted in two important ways. First, if a section 304(a) criterion is translated into the concentration component of a water quality standard, scientific considerations specific to a given water body may be taken into account. A criterion which has been established as generally necessary to support a specified use may not be required to maintain that use in a particular water body. For example, in some cases ecosystem adaptation may enable a viable balanced

aquatic population to exist in waters with high natural background levels of certain pollutants. Similarly, toxicity of certain compounds may be less in some waters because of differences in acidity, temperature, water hardness, and other factors. (Conversely, some natural water characteristics may increase the impact of certain pollutants.)

Second, a section 304(a) criterion adopted by a State or federally promulgated under section 303 acquires regulatory weight only when a particular water body is designated for the use which the criterion is designed to protect. A water body designated for agricultural use, for example, might not have to achieve the same concentration levels as a water body designated for the protection and propagation of fish, shellfish, and wildlife. The criteria issued today which reflect levels for the protection of aquatic life and human health would not necessarily be required to protect other uses such as agriculture.

EPA has established regulations and policies concerning section 304(a) water quality criteria and section 303 concentrations and uses. This program was summarized in the ANPRM, and public comment was invited on a variety of questions about the direction this program should take in the future.

Issues raised in the ANPRM potentially affect the significance of the criteria issued today. For instance, EPA's policy for its current (1976) water quality criteria (the "Red Book" criteria) is that "a State may adopt a numerical concentration for a Red Book pollutant which is less stringent than the Red Book number, but only if a State provides adequate technical justification for the deviation." (43 FR at 29590) Failure to provide adequate technical justification may result in EPA disapproval of that portion of the water quality standard and, subsequently, in EPA proposal and potential promulgation of the more restrictive limit. The Agency is considering extending this policy concerning Red Book criteria to its new toxic pollutant criteria after such criteria are published as final, and solicits comments on this option.

The ANPRM also stated that it is EPA's current policy generally not to promulgate standards for pollutants which States have not addressed in their standards. As stated in that notice, EPA is contemplating altering this policy for some or all of the 65 toxic pollutants. Thus, EPA might "provide a list of pollutants for which water quality standards must be developed" either by the States or by EPA (43 FR at 29591). This policy will be developed in future rulemaking efforts separate from the issuance of water quality criteria for public comment today. Persons wishing to comment on this policy option will therefore be able to make their views known at that time.

Relationship to Drinking Water Standards

It is not expected that health-based water quality criteria will necessarily be the same as standards or guidelines issued by EPA under other Acts since other authorities may mandate different considerations. The mandate for establishing standards for drinking water at the tap under the Safe Drinking Water Act (SDWA), for instance, expressly requires consideration of economic and technical feasibility, whereas feasibility is not a factor in developing section 304 water quality criteria. In addition the extrapolation model used to estimate the risk associated with the Interim Primary Drinking Water Standards was somewhat different from that used in calculating water quality criteria. Thus, the criteria today are not intended to serve as drinking water tap standards. Nor are today's criteria expected to be the same as recommended maximum contaminant levels (RMCL's), non-enforceable health-based goals, which are also mandated under the SDWA. While RMCL's are more like section 304 criteria than tap water standards, specific mandates of the SDWA such as the consideration of multi-media exposure, as well as the different methods for setting contaminant levels under the two Acts may result in differences between RMCL's and the criteria published for comment today. In the future, a State or EPA may through rulemaking proceedings consider using the health-based section 304(a) criteria for a public water supply designated use standard under section 303. In such a case, consideration may be given to whether pollutants are more effectively removed before they reach the ambient water (i.e., at the point of discharge), or at a drinking water treatment works.

Development of the Criteria

The development of water quality criteria reflecting the latest scientific knowledge is necessarily an ongoing process. Section 304 reflects awareness of this fact in its requirement that criteria periodically be revised. As new information becomes available indicating that an existing criterion should be revised, or that criteria should be established for substances which have not yet been addressed, it is expected that new or revised criteria will be developed. The draft criteria issued for comment today are part of this ongoing program. It should be recognized therefore that, when published after public comment, these criteria will not be "cast in concrete" but will be updated in future years when additional information becomes available indicating such a need.

EPA recognizes that the quality and quantity of the data in the criteria documents varies, and has undertaken a program to expand the data base dealing with bioconcentration factors and aquatic toxicity. Further data generation can be expected in the future. Comment is invited on what constitutes a sufficient data base for final criterion formulation and on how the quality of the criteria may best be expressed.

The criteria issued for comment today are of two basic kinds: (1) Concentrations estimated to be protective of aquatic life and wildlife, and (2) concentrations relevant to the protection of human health. Criteria are not now being issued to protect recreation, agricultural or industrial uses, since a general lack of data precludes such an effort at this time. As data become available, however, appropriate criteria will be developed. The pollutants covered by today's documents are listed in Appendix A along with summaries of the criteria formulation for each pollutant.

The criteria for protection of aquatic life and wildlife and criteria for the protection of human health were derived separately from essentially different data bases utilizing methods designed specifically to address the concerns of the two separate areas. The methods for deriving criteria in each

of these areas are presented in appendices B and C, and are discussed briefly below. Comment is invited on all aspects of the methods used and their application in the development of specific criteria.

CRITERIA FOR THE PROTECTION OF AQUATIC LIFE

Most of the aquatic life criteria issued for comment today were derived using guidelines developed from data for a wide range of pollutants and organisms to provide a systematic and consistent approach to the derivation of aquatic life criteria. These guidelines were presented for public comment on May 18, 1978 (43 FR 21506), and over 50 comments were received. As explained in that notice, the guidelines "provide uniform rules for deriving criteria from data bases (for individual pollutants) of varying degrees of adequacy and supply rules for estimating some effects for which data are unavailable." (43 FR at 21506) In a few instances the guidelines were modified on a case-by-case basis where pollutant-specific data indicated both the need and the direction for such modification. Criteria so derived are identified in the text, and the reasons for any modification explained. For some pollutants, data needed to formulate criteria following the guidelines were not available but could be estimated using alternative procedures. In these cases criteria were derived using alternative methods. Finally, where data on a particular pollutant were not sufficient to derive criteria using the guidelines or the alternative procedures, no criterion is presented.

Since a detailed explanation of the basic guidelines is presented in the May 18th notice, interested persons should refer to that notice as modified in appendix B for a basic understanding of the derivation of aquatic life criteria. appendix B contains clarifications which resulted from application of the guidelines as well as a summary of the althernative methods by which criteria are derived.

In the May 18th notice EPA stated its intent to refine the guidelines in response to public comment before issuing these criteria for public comment. Because of the magnitude of the task of preparing these criteria documents within a limited time frame, and because of the highly detailed and technical nature of the guidelines and the numerous comments thereon, however, no major refinements to the guidelines have yet been completed. The criteria issued today, therefore, follow the guidelines published in May, modified as noted in appendix B to reflect knowledge gained in application of the guidelines to the individual data bases. Also, as noted, case-by-case modification and alternative methods have been employed where appropriate.

The complex nature of the guidelines has also compelled EPA to defer response to comments on the May 18th notice at this time. A summary of the comments is presented in Appendix D, however, to assist the reader in understanding the general outlines of the response to the guidelines and the direction which further work on the guidelines is taking.

In order to respond to comments on the May 18th notice EPA has undertaken an assessment of the technical and scientific foundations of the guidelines. This task involves extensive reformatting of the data base and inclusion of new references, as well as investigation of appropriate groupings of data to estimate correction factors used to standardize results and the effects of their variability; enhanced quantification of the variability in the standardized data base; assessment of the validity of averaging across toxicant and species groups; investigation of the sensitivity of criteria to data requirements; and consideration of alternatives for estimating criteria including the use, where appropriate, of regression models, application factors and dose-response bioassay models.

It should be noted that this assessment effort and comments received on the documents issued today may indicate a need for changes in the derivation methods or their application in individual cases. Where modification is so indicated, the derivation methods and criteria values in the final documents may differ from those issued for comment today. The reasons for any modifications will accompany the final documents.

Since the guidelines assessment task will extend into the comment period on today's criteria documents, comments on the guidelines not previously submitted will be accepted during this period. It is not necessary to repeat any comments previously submitted in response to the May 18th notice, as they are already being considered in the reanalysis. A comprehensive response to major substantive comments will accompany the final publication of the documents.

Although response to comments on statistical and toxicological aspects of the guidelines must await completion of the guidelines assessment, two more general aspects of the guidelines which raised some questions are further discussed here. The first aspect which may require some clarification is the twofold nature of the aquatic life criteria. These criteria are comprised of a recommended average concentration not to be exceeded during any 24-hour period and a recommended maximum or ceiling concentration which should not be exceeded at any time during the 24-hour period. The average figure represents a concentration estimated to protect against adverse chronic effects. It is presented as an average because chronic data are usually based on tests lasting from several weeks to more than a year, during which the pollutant concentrations vary. Thus some fluctuation is inherent in a mean exposure concentration, and aquatic organisms can be expected to tolerate some excursions over this mean so long as the excursions are not too high or too frequent.

A time period of 24 hours was chosen in order to ensure that concentrations not reach harmful levels for unacceptably long periods. Averaging for longer periods, such as a week or a month for example, could permit high concentrations to persist long enough to produce significant adverse effects. A 24-hour period was chosen instead of a slightly longer or shorter period in recognition of daily fluctuations in waste discharges and of the influence of daily cycles of sunlight and darkness and temperature on both pollutants and aquatic organisms.

Merely specifying an average is insufficient, however, because data show that very high concentrations of chemicals can kill or cause irreparable damage in very short periods. Furthermore, for some chemicals the effect of intermittent high exposures is cumulative. It is therefore necessary to place an upper limit on concentrations over the average value.

The use of a ceiling value based on

96-hour LC50 data was a practical choice. Much of the available acute toxicity data are for 96 hours and the time-concentration mortality curves are poorly documented for shorter periods. Also the additive effect of intermittent exposures mentioned above suggest that higher concentrations might cause harm. It is believed that the values derived from 96-hour LC50 concentrations will be protective against acute toxicity during short excursions from the 24-hour average chronic criterion.

In sum, the two-number criterion is intended to describe an ambient water concentration which will produce an average water quality generally suited to the maintenance of aquatic life while restricting the excursions over that average to levels which will not cause harm.

A second point of concern to commenters was the possibility of using the guidelines to develop criteria taking into account specific water body characteristics. Several commenters noted that the guidelines were presented as making such water-body-specific criteria possible, but that the manner in which this would be achieved was not elaborated.

The criteria issued today should make this feature clearer. A major advance in specificity, for instance, is that to the extent possible criteria are separately derived for salt and fresh waters. In another effort to take specific characteristics into account, criteria for compounds whose toxicity varies markedly with various degrees of hardness are presented in the form of curves. Although EPA recognizes that other water characteristics such as pH, temperature, or degree of salinity (as in estuaries) may affect the toxicity of some pollutants, the data base at this time is not detailed enough to allow for further specificity. The guidelines constitute a structure by which such information may be used for deriving section 304 criteria as it becomes available. This structure will also allow States or EPA to take these variables into account, where data permit, when setting enforceable standards through rulemaking in the future.

Criteria for the Protection of Human Health

The objective of the health assessment portions of the criteria documents is to estimate ambient water concentrations which, in the case of non-carcinogens, represent "safe" levels for humans, and in the case of suspect or proven carcinogens, represent various levels of incremental cancer risk.

Health assessments follow general guidelines developed to assist the scientist in identifying and interpreting all pertinent data on the subject pollutant without impeding the exercise of scientific judgment and expertise. These guidelines are presented in Appendix C.

Health assessments typically contain four elements: Exposure, pharmacokinetics, toxicity, and criterion formulation. The exposure section summarizes information on possible exposure routes such as ingestion, inhalation, and dermal contact. The pharmacokinetics section reviews data on absorption, distribution, metabolism and excretion to assess the biochemical fate of the compounds in the human and animal system. The effects section reviews acute, subacute, and chronic toxicity, synergistic and antagonistic properties, and specific information on mutagenicity, teratogenicity and carcinogenicity. From this review the toxic effect to be protected against is identified, taking into account the quality, quantity and weight of evidence characteristic of the data. The last section presents the data analysis and rationale for criterion development and the mathematical derivation of the criterion.

Specific criteria are developed only if a weight of evidence supports the occurrence of the toxic effect and if dose/response data exist from which criteria can be estimated. Criteria for suspect or proven carcinogens are presented as concentrations in water associated with a range of incremental cancer risks in man. Criteria for non-carcinogens represent levels at which exposure to a single chemical is not anticipated to produce adverse effects in man. In a few cases organoleptic (taste and odor) data form the basis for the criterion because chronic toxicity data were either lacking, insufficient or resulted in a level higher than that which produced adverse organoliptic effects. Finally, for a few toxicants no criteria are recommended due to a lack of information sufficient for quantitative criterion formulation.

Most criteria are based on exposure directly through consumption of water containing a specified concentration of a toxic pollutant and indirectly through consumption of aquatic organisms which may bioconcentrate pollutants from the waters in which they live. In addition to providing a range of concentrations estimated to pose specified risks of cancer from the consumption of water and edible aquatic organisms, the carcinogen documents present a range of concentrations corresponding to risk incurred from the consumption of edible aquatic organisms alone. In the latter case, it is assumed that water consumed by an individual would not contain the pollutant in question. In criteria reflecting both the water consumption and aquatic organisms routes of exposure, the relative contribution varies with the propensity of a pollutant to bioconcentrate, with the consumption of aquatic organisms becoming more important as the bioconcentration factor (BCF) increases. When the BCF is 100, for example, exposure through the two routes is roughly equal. At higher BCF's such as 1,000 to 100,000, the contribution of the water consumption route becomes relatively minor.

For a few pollutants, information about exposure from other sources such as air or non-aquatic diet has been considered in formulating criteria. These situations are explained in the individual documents.

As information on total exposure is assembled for pollutants for which criteria reflect only the two indicated exposure routes, adjustments in water concentration values may be made. It is anticipated that future revisions of health-based criteria will contain more information on additional exposure routes.

Within the limitations of time and resources, all up-to-date published information of significance is incorporated into the assessments. Review articles and reports are used for data evaluation and synthesis. Scientific judgment is exercised in reviewing and evaluating the data in each document and identifying the adverse effects for which protective criteria are sought.

Guidelines and Assumptions

A uniform approach to criteria for-

mulation has been developed using the following basic assumptions and guidelines. The assessment of health risks associated with human exposure to environmental pollutants requires predicting the effect of low doses for up to a lifetime in duration. Because in most cases adequate data on toxic effects in humans are not available due to ethical and practical considerations, predictions are usually made by extrapolation from animal data. However, valid clinical and epidemiological studies are used for both qualitative and quantitative evaluation wherever available. A combination of epidemiological and animal dose/response data was considered the preferred basis for quantitative criterion development.

No-effect or specified risk concentrations were estimated by extrapolation from animal toxicity or human epidemiology studies using the following basic exposure assumptions: a 70-kilogram male person ("Report of the Task Group on Reference Man", International Commission for Radiation Protection, November 23, 1975) as the exposure individual; the average consumption of specified fish and shellfish products equal to 18.7 grams/day (Health Perspectives 24:157-172); and the average ingestion of two liters/day of water ("Drinking Water and Health", National Academy of Sciences, National Research Council, 1977). Concentrations based on these assumptions are estimated to be protective of an adult male who experiences average exposure conditions.

For carcinogens, the method of extrapolation from high dose to low dose effects produces health risk and associated concentration levels which are least likely to understate the human risk. For noncarcinogens, concern that extrapolated values may be underprotective is minimized by the use of safety factors of 10, 100, and 1,000. Special subpopulation sensitivities and synergistic effects are not typically factored into the criteria, although they are referenced, if known. The use of upper bound and otherwise cautious estimation methods is believed to compensate at least partially for the absence of specific consideration of these factors.

Human intake of pollutants from consumption of aquatic organisms is estimated using bioconcentration factors (BCF's) along with the average weight of fish and shellfish products consumed daily. Since BCF's generally are not available for edible portions of freshwater and marine species normally consumed in the U.S., procedures have been developed to estimate edible portion BCF's from whole fish BCF's and from octanol-water partition coefficients. For organic pollutants, for which the BCF is generally proportional to the percentage of lipids in the organism, whole species BCF's are adjusted to edible portion BCF's using data on the percent of lipids in various species and the amounts of those species consumed by the population. For inorganic contaminants, specifically metals, for which the BCF depends on the physical and biological characteristics of the aquatic species, BCF's are estimated by taking a weighted average of the known BCF data.

Two basic methods were used to formulate health criteria, depending on whether the target effect was cancer or other toxic manifestations. Determinations of carcinogenicity were made following the principle that any substance which is shown to cause tumors in animals should be considered a suspect carcinogen and therefore a potential hazard for man. Exceptions were considered only where the carcinogenic effect is clearly shown to result from physical rather than chemical induction, or where the route of administration is shown to be inappropriate in terms of conceivable human exposure. These determinations were reviewed by EPA's Cancer Assessment Group.

Carcinogens

Because methods do not now exist to establish the presence of a threshold for most, if not all, carcinogenic effects, EPA's policy is that there is no scientific basis for estimating "safe" levels for carcinogens. The draft criteria for carcinogens therefore state that the recommended concentration for maximum protection of human health is zero. In addition, the documents present a range of concentrations estimated to pose various degrees of incremental "cancer risk." For example, a document might indicate that exposure to a carcinogen through the lifetime daily consumption of water and edible aquatic organisms could result in one additional case of cancer in a population of 1,000,000 at a concentration of 0.1μg/l, and of 1 additional cancer in a population of 100,000 at a level of 1.0μg/l. Other risk-concentration pairs may be calculated by simple extrapolation.

This range of risk estimates is presented for information purposes and does not indicate any "acceptable" risk level, since as noted the only known exposure guaranteeing maximum protection of human health is zero. However, because in many situations the achievement of zero levels may be infeasible at this time, it may be necessary to identify a maximum target risk level to be recommended in the interim. The Agency is considering a level in the range of 10^{-7} to 10^{-8} as such a target. Concentrations corresponding to the target risk level would become a part of the criteria used by States and EPA for developing and reviewing water quality standards. It should be recognized that particular circumstances may call for the recommendation of risk levels of greater stringency than the target. Such circumstances might exist, for example, where significant exposure to a particular pollutant occurs through other routes, or where several potential carcinogens are present in the same water. Also, as noted above, feasibility and other considerations taken into acount in applying the criteria in section 303 or other regulatory standards may result in enforceable standards which pose a less stringent level of risk. EPA invites public comment on the desirability of establishing an interim target risk level, and on the level at which such a target should be set.

Risk assessment from animal data is performed using the "one-hit" model recommended in the Agency's Interim Cancer Procedures and Guidelines for Health Risk and Economic Impact Assessments of Suspect Carcinogens (41 FR 21402, May 29, 1976). The model has been modified to acount for spontaneous tumor incidence and to adjust for tumors not observed because of premature, chemical-induced death. EPA is aware that other models for risk extrapolation exist and have been used by EPA under other Acts, as well as by other Federal agencies. The "one-hit" model has recently been endorsed by the four agencies in the Interagency Regulatory Liaison Group. It is one of the most conserva-

tive models available, since it is less likely to underestimate risk at the low doses typical of environmental exposure. Because of the uncertainties associated with dose and animal-to-human extrapolation and other unknown factors, because of the use of average exposure assumptions, and because of the serious public health consequences that could result if risk were underestimated, EPA believes that it is prudent to use conservative methods to estimate risk in the water quality criteria program.

It should be observed that extrapolation models provide only rough estimates of risk since a variety of assumptions are built into any model. Models using widely different assumptions may produce estimates ranging over several orders of magnitude. Since there is at present no way to demonstrate the scientific validity of any model, the use of risk extrapolation models is a subject of debate in the scientific community. However, risk extrapolation is generally recognized as the only tool available at this time for estimating health hazards associated with suspect non-threshold toxicants and has been endorsed by EPA and other agencies as a useful means of assessing the risks associated with various chemicals.

Risk assessment based on extrapolation from epidemiological dose-response data is made by direct proportionality estimates from the levels of exposure to pollutants and the related incidence of cancer in man.

If data permit, assessments are based on data in which the tumor incidence resulted from ingestion of the particular compound. However, data from animals or humans exposed by other routes are used where ingestion data are lacking and there is no indication that the mode of toxicity is route-specific.

Other Adverse Effects—Non-Carcinogenic Effects

Health criteria based on toxic effects of pollutant other than carcinogenicity are estimates of concentrations which are not expected to produce adverse effects in humans. They are termed Acceptable Daily Intake (ADI) levels and are generally derived using no-adverse-effect data from animal studies although human data are used wherever available. The ADI is calculated using factors to account for uncertainties inherent in extrapolation from animal to man. In accordance with the National Research Council recommendations ("Drinking Water and Health", National Academy of Sciences, National Research Council, 1977), uncertainty factors of 10, 100, or 1,000 are used depending on the quality and quantity of data. In some instances extrapolations are made from inhalation studies or limits to approximate a human response from ingestion using the Stokinger-Woodward model (Journal of American Water Works Association, 1958). Calculations of criteria from ADI's are made using the standard exposure assumptions (2 liters of water, 18.7 grams of edible aquatic products and an average body weight of 79 kg).

Specific Issues for Commenters To Address

Written public comment is invited on all issues raised by this notice as well as any other issues concerning the development of water quality criteria under the Act. Comments should be sent to Kenneth M. Mackenthun at the address noted in the introduction to this notice.

EPA is especially interested in comments on the following issues:

1. The advisability of extending the current Red Book policy on the justification of less stringent criteria to some or all of the 65 toxic pollutant criteria.
2. The scientific validity and appropriateness of the aquatic guidelines and the alternative procedures set forth in Appendix B. (NOTE: Comments previously submitted in response to the May 18 notice should *not* be repeated.)
3. The scientific validity and appropriateness of the methods used for deriving health-based criteria presented in Appendix C.
4. The size, nature, and quality of data bases used for deriving criteria.
5. The application of criteria derivation methods to particular pollutants.
6. The use of risk extrapolation for deriving criteria for suspect or proven carcinogens.
7. The establishment and appropriate use of an interim target risk level.
8. The level at which such a target should be set.

Availability of Documents

Summaries of both aquatic-based and health-based criteria and the criteria formulation sections of the documents are published below. Copies of the complete documents have been sent to all persons who have requested copies to date, as well as to those who commented on the May 18th notice. Other persons wishing to review the full documents may obtain copies for individual pollutants from the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia (703) 557-4650. The documents are also available for public inspection and copying during normal business hours at: Public Information Reference Unit, U.S. Environmental Protection Agency, Room 2404 (rear), 401 M Street, SW., Washington, D.C. 20460. As provided in 40 CFR Part 2, a reasonable fee may be charged for copying services. Copies of these documents will also be available for review in the EPA Regional Office libraries.

Dated: February 28, 1979.

Douglas M. Costle,
Administrator.

Appendix A

Arsenic and Compounds

Criteria Summary:

Freshwater Aquatic Life

For arsenic, the criterion to protect freshwater aquatic life, as derived using the Guidelines, is 57μg/l as a 24 hour average and the concentration should never exceed 130μg/l at any time.

Saltwater Aquatic Life

For arsenic, the criterion to protect saltwater aquatic life, as derived using procedures other than the Guidelines, is 29μg/l as a 24 hour average and the concentration should never exceed 67μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to arsenic through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of arsenic estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this doucment. The Agency is considering setting criteria at an interim target risk level in the

range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of .02μg/l, .002μg/l, and .0002μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of arsenic is the Final Acute Value of 130μg/l which is based on the more acutely sensitive invertebrate organisms. Since 0.44 times the Final Acute Value is lower than the Final Chronic Value (170μg/l), the former is the 24-hour average concentration.

For arsenic the criterion to protect freshwater aquatic life as derived using the Guidelines is 57μg/l as a 24-hour average and the concentration should not exceed 130μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of arsenic.

Final Fish Acute Value=4,400μg/l
Final Invertebrate Acute Value=130μg/l
Final Acute Value=130μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=170μg/l
Final Plant Value=2,300μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=170μg/l
0.44 x Final Acute Value=57μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for arsenic using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available. Data for arsenic and freshwater organisms can be used to estimate a criterion.

For arsenic and freshwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from results of a life cycle test with *Daphnia magna*. Therefore, a reasonable estimate of a criterion for arsenic and saltwater organisms would be 0.44 times the Final Acute Value.

The maximum concentration for arsenic is the Final Acute Value of 67μg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For arsenic the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 29μg/l as a 24-hour average and the concentration should not exceed 67μg/l at any time.

Summary of Availability Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of arsenic.

Final Fish Acute Value=1,400μg/l
Final Invertebrate Acute Value=67μg/l
Final Acute Value=67μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=580μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=580μg/l
0.44 x Final Acute Value=29μg/l

Human Health

A number of studies have shown that arsenic is important in the etiology of human cancers. Clinical, occupational, and population studies have demonstrated that both ingestion and inhalation exposures to arsenic compounds increase the risk of cancer induction in the tissues of the lung and skin and possibly other sites. There appears to be little question that arsenic is a human carcinogen, but there has been general failure to demonstrate this effect in any animal model. Hence, it is necessary to rely totally on human data rather than supplement it with appropriate animal toxicity and carcinogenic data. This limitation causes serious problems since animal studies are the only practical means to effectively evaluate relative toxicities, absorption rates, etc. for different compounds and routes of administration. Instead, these types of questions must be answered based on effects and observations of exposed populations recognizing the numerous unknowns (levels or arsenic and other environmental exposures, dietary patterns, genetic differences, etc.) and different routes of exposure.

A study that relates levels of arsenic ingestion to skin cancer was conducted in southwest Taiwan. A consistent dose response relationship between the exposure variables level of arsenic in drinking water and age and skin cancer prevalence was found. Questions concerning compatibility between the U.S. and Chinese populations must be raised since some areas in the U.S. have similar arsenic levels without the reported dermatological manifestations. It is very possible that major differences in dietary patterns (the Chinese diet is low in protein and fat) other environmental and/or occupational co-exposures, socio-economic status, etc, may account for the differences. However, since similar health responses have been observed in Antofagasta, Chile; Cordoba, Argentina; German vineyard workers, and those who ingest Fowler's Solution, it must be assumed that arsenic is at least one of the environmental exposures responsible for the observed effects.

Secondly, the clear dose response relationships both by length of exposure, as indicated by age, and by level of waterborne arsenic provide additional evidence that arsenic is at least one of the agents responsible for the observed effects; it seems quite unlikely that other environmental, occupational, or socio-economic factors which might be responsible for variations in skin tumor incidence would have a similar gradient to the waterborne arsenic gradient. Hence, it appears reasonable to use the Taiwan data as a basis for estimating a level which will not increase the lifetime risk of cancer by more than 1/100,000; it is recognized the calculated level may be quite conservative since the Taiwan experience may represent a worst case situation due to other co-exposures and dietary deficiencies.

The EPA Cancer Assessment Group has developed a mathematical prediction model for estimating an acceptable level based on the published Taiwan data (Tseng, 1977).[1]

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and

[1]Tseng, W. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. Environmental Health Perspective, 19:109.

recreational activities." Arsenic is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of arsenic in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of arsenic corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria[1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.0002	0.002	0.02
Consumption of fish and shellfish only	0	0.01	0.10	1.0

[1] Calculated by applying a modified "one-hit" extrapolation model to the human epidemiological data presented in Summary to Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately 2 percent of the arsenic exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 2.3 fold. The remaining 98 percent of arsenic exposure results from drinking water.

Summary of Pertinent Data

Due to the stable population in a rural area along the southwest coast of Taiwan, the data collected by Tseng et al. in 1968 [3] may be viewed as a lifetime feeding study where measured amounts of arsenic in well water are consumed by a study population of 40,421 individuals. Thus, this data may be used to predict the lifetime probability of skin cancer caused by the ingestion of arsenic.

A model estimating the cancer rate as a function of drinking water arsenic concentration was generated using the information in its published form, which is a summary of data collected by the investigators. If the original data had been available, a more exact mathematical analysis would been possible.

It has been suggested that the relationship between the incidence of some site specific cancers, age, and exposure level of a population may be expressed as

$$(1)\ I(x,t)=vBx^{m}t^{v-1}$$

where x is the exposure level of a carcinogen, t is the age of the population, and B, m, v are unknown parameters.

However, the data collected by Tseng et al. in 1968 [3] was obtained at one point in time, and since skin cancer has only a marginal effect on the death rate, the obtained rates may be viewed more accurately as the probability of having contracted skin cancer by time t. The relationship between this probability, often referred to as the cummulative probability density or prevalance, and the incidence or age specific or hazard rate may be expressed as

$$(2)\ F(x,t)=1-\exp[\int I^{v}(x,s)\,ds]$$

Utilizing the suggestion of Doll (1971) for the form of the incidence rate, the prevalence may be expressed as

$$(3)\ F(x,t)=1-\exp(-Bx^{m}t^{v})$$

which is a Weibull distribution.

Based on information reported by Tseng et al. in 1968 [3], we have estimates of F (x,t) for different age and exposure groupings for males.

To use this data, specific values for x and t had to be obtained for the intervals. Where the intervals were closed the midpoint was utilized. For the greater than .6 mg/1 group the midpoint between .6 and the greatest recorded value 1.8 was taken resulting in 1.2 μg/l. For age 60 or greater, a value of 70 was utilized somewhat arbitrarily, being the same increase over the lower level as that in the other two age intervals.

From equation (5) it follows that

$$(4)\ \ln(-\ln[1-F(x,t)])-\ln(3)+m\ln(x)+v\ln(t)$$

which is multiple linear in form. Estimating the parameters by the usual least square techniques, we obtained the relationship

$$(5)\ \ln(-\ln[1-F(x,t)])=-17.548+1.192\ln(x)+3.881\ln(t)$$

which is an excellent fit having a multiple correlation coefficient of 0.986.

Equation (5) may be expressed as

$$(6)\ F(x,t)=1-\exp[-10^{-7}\times.2429\,x^{1.192}t^{3.881}]=1-\exp[-E(t)\,x^{1.192}]$$

If the coefficient m = 1.192 was in fact equal to 1, then for a given value of t equation (6) would be "one-hit" in form.

To test this hypothesis, (i.e. Eo: m=1) the student "t" test is used, giving the result

$$t_6=\frac{1.192-1}{1.138}=1.391$$

which is not significant at the .1 level. The value 0.138 is the standard error of m. Thus there is insufficient evidence to reject the hypothesis that the dose response relationship is "one-hit" even at the 0.1 level even though the standard error of the regression coefficient is quite small.

Fixing m=1 we have the relationship

$$(7)\ F(x,t)=1-\exp[g(t)x]$$

Transforming this equation to its linear form and obtaining the least square estimates of B and v, we find that

$$g(t)=\exp(-17.5393)\,t^{3.853},\ \text{where}\ B=2.41423\times10^{-8},\ v=3.853$$

In this case, the fit is still quite good as represented by a correlation of 0.971.

The function $F(x,t)=1-\exp[-2.41423\ 10^{-5}\times t^{3.853}]$, is the probability of contracting skin cancer by age t given that an individual had a lifetime exposure to x mg/1 in his drinking water (and lived until age t).

In a 1978 U.S. Environmental Protection Agency document the lifetime probability of cancer in the presence of competing mortality was derived from the age-specific incidence rate. For the case where the cancer rate in the absence of exposure is near zero (as in this case where the skin cancer is of a rare form that was virtually unknown in other parts of Taiwan) the lifetime probability may be expressed as

$$Q_x(\ )=Bx/(Bx+p^v)$$

where $p^v=\ln 2\ t_m^v$, (where t_m is the median lifetime of the population). Assuming $t_m=68$ and $v=3.853$, is the same for total mortality as the appearance of skin cancer we have that

$$\frac{Q_x(\ )=2.41423\times}{2.41423\times+6.02793}$$

The level of x that results in a lifetime probability of skin cancer equal to 10^{-5} is found by solving $Q_x(\ )=10^{-5}$ for x giving $x=2.4969\times10^{-5}$ µg/liter or 0.025 µg/liter.

Under the assumption that the average consumption of water is two liters in both the U.S. and Taiwan we estimate a water criteria concentration of:

$$2(.025)=S(2+.0187\times 2.3)\ \underline{or}$$

$$S=\frac{.05}{2.0430}=.02447$$

Where .0187 is the average fish consumption in kilograms and 2.3 is the bioaccummulation factor for fish (supplied by Don Mount of U.S. EPA).

A criterion for waterborne arsenic of .02 µg/l would thus insure a lifetime risk of cancer of less than 10^{-5}.

It is recognized that inorganic and organic compounds differ in terms of toxicity and likely in terms of carcinogenic potential. However, since the recommended level is to be based on carcinogenic potential and no information is available concerning the relationship(s) of specific arsenic species and cancer a single all inclusive limit must be set. Even if the data were available to permit separate standards, the level of development of the required analytical methodology is not sufficient to permit reliable and repeatable speciation measurements, a necessity before setting a standard.

For comparative purposes, the Stockinger and Woodward method was applied to the present and proposed airborne arsenic standards to compute comparable waterborne arsenic levels.

American Conference of Governmental Industrial Hygienists:

1. Existing Threshold Limit Value—Time Weighted Average—500µg/m³

$$\frac{500\ \mu g}{m^3}\times 10\ m^3\times\frac{5\ days}{week}\times 20\%\ absorption = 5{,}000\ \mu g/liter$$

$$\frac{5000\ \mu g}{week}\times\frac{1\ week}{7\ days}\times\frac{1}{2\ liters}\times\frac{Allowed}{80\%\ absorption} = 446\ \mu g/liter$$

Applying the recommended safety factor of 1/100 the comparable drinking water limit is 4.46 µg/liter.

Proposed Threshold Limit Value—Time Weighted Average —50µg/m³

$$\frac{50\ \mu g}{m^3}\times 10\ m^3\times\frac{5\ days}{week}\times 20\%\ absorption = 500\ \mu g/wk$$

$$\frac{500\ \mu g}{week}\times\frac{1\ week}{7\ days}\times\frac{1}{2\ liters}\times\frac{Allowed}{80\%\ absorption} = 44.6\ \mu g/liter$$

Applying the recommended safety factor of 1/100 the comparable drinking water limit is 0.45µg/liter.

Occupational Safety and Health Administration

1. Eight-hour average —10µg/m³

$$\frac{10\ \mu g}{m^3}\times 10\ m^3\times\frac{5\ days}{week}\times 20\%\ absorption = 100\ \mu g/week$$

$$\frac{100\ \mu g}{week}\times\frac{1\ week}{7\ days}\times\frac{1}{2\ liters}\times\frac{Allowed}{80\%\ absorption} = 8.93\ \mu g/liter$$

Applying the recommended safety factor of 1/100, the comparable drinking water limit is 0.08µg/liter.

Assuming that the absorption factors (air—20%, water—80%) and methods recommended by Stockinger and Woodward are reasonable and that the safety of 1/100 is appropriate, it is clear that the recommended water standard is even more restrictive than the air standards. The differences are likely due at least partially to variations in extrapolation methods and levels of acceptable risk.

It is of interest to see what cancer risk would be associated with an air exposure equivalent to the recommended criterion of .02µg/l. If we make the following assumptions:

(1) Total daily average absorbed arsenic from water is $.8\times.02(2\div.0267\times15)=.038\Delta\mu g$, where 80% is the absorption rate.

(2) The breathing rate is 1m³/hr and 20% of the arsenic is absorbed.

Concentration levels were derived assuming a lifetime exposure to various amounts of arsenic, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding arsenic concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding arsenic concentrations.

Although total exposure information for arsenic is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into ambient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assumed an incremental risk from ambient water exposure only.

Then, the air concentration, X, required to obtain the same absorbed amount of arsenic is

$$.2\times24\times X=.0384\ mg\ or\ X=.008\mu g/m^3$$

From the 1978 U.S. Environmental Protection Agency document on the risk associated with airborne arsenic the lifetime cancer risk associated with $X\mu g/M^3$ of arsenic in the air is estimated to be

$$P=3.418\times10^{-3}X$$

If instead of basing our risk on the most sensitive study we use the geo-

metric mean of the three studies the lifetime cancer risk would be

$$P=1.95\times10^{-3}X$$

The risks associated with X=.008 are thus 2.73×10^{-5} and 1.56×10^{-5}. Thus if our water criterion was based on the geometric mean of the human epidemiological air studies it would be .013μg/l instead of .02μg/l, which is remarkably consistent result.

Criteria Summary:

Freshwater Aquatic Life

For benzene the criterion to protect freshwater aquatic life as derived using the Guidelines is 3,100μg/l as a 24-hour average and the concentration should not exceed 7,000μg/l at any time.

Saltwater Aquatic Life

The data base for saltwater aquatic life is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data for freshwater organisms.

For benzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 920μg/l as a 24-hour average and the concentration should not exceed 2,100μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to benzene through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of benzene estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the criterion formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 15μg/l, 1.5μg/l, and 0.15μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration is the Final Acute Value of 7,000μg/l and the 24-hour average concentration is 0.44 times the Fial Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For benzene the criterion to protect freshwater aquatic life, as derived using the Guidelines, is 3,100μg/l expressed as a 24-hour average and the concentration should not exceed 7,000μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=7,000μg/l

Final Invertebrate Acute Value=8,200μg/l

Final Acute Value=7,000μg/l

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=greater than 19,000μg/l

Final Plant Value=530,000μg/l

Residue Limited Toxicant Concentration=not available

Final Chronic Value=greater than 19,000μg/l

0.44×Final Acute Value=3,100μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for benzene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, results obtained for benzene with freshwater organisms indicate how a criterion may be derived. For benzene and freshwater organisms the Final Chronic Value based on *Daphnia magna* is greater than 0.44 times the Final Acute Value. Therefore, it seems reasonable to derive a criterion for benzene and saltwater organisms using 0.44 times the Final Acute Value.

The maximum concentration is the Final Acute Value of 2,100μg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration other than those noted earlier.

For benzene, the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 920μg/l as a 24-hour average and the concentration should not exceed 2,100μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=2,400μg/l

Final Invertebrate Acute Value=2,100μg/l

Final Acute Value=2,100μg/l

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=not available

Final Plant Value=20,000μg/l

Residue Limited Toxicant Concentration=not available

Final Chronic Value=20,000μg/l

0.44×Final Acute Value=920μg/l

Human Health

The Natl. Acad. Sci./Natl. Res. Coun. in its review of drinking water and health, concluded that existing animal and human data did not allow the establishment of limits for benzene in drinking water. This was because the animal results were not statistically significant and were based on non-oral administration of benzene. In addition, the occupational studies on human exposure did not contain adequate information on degree of exposure or size of the population at risk, and did not rule out exposure to other chemicals besides benzene.

Since the publication of the Natl. Acad. Sci./Natl. Res. Coun. report, epidemiological studies by Aksoy, Infante, et al. and Ott, et al. have appeared. These studies include information on degree of benzene exposure and size of the population at risk, and rule out exposure to solvents other than benzene. The U.S. EPA Carcinogen Assessment Group has made use of these three occupational studies to calculate a leukemia dose-response curve. The slope of this curve is 0.024074, in units of lifetime risk of leukemia per ppm exposure to benzene in air. Since 1 ppm is 3.25 mg/m³, and assuming a respiratory rate of about 24 m³/day, the benzene intake per individual at 1 ppm is:

$$(3.25\ mg/m^3)(24 m^3/day)=78\ mg/day$$

To calculate the benzene intake resulting in a lifetime risk of leukemia of 10^{-5}, one solves the following equation for x,

$$\frac{x}{10^{-5}} = \frac{78\ mg/day}{0.024074}$$

Resulting in 0.032 mg/day.

The U.S. EPA total exposure analysis indicates that the total body exposure may be as high as 1.1 mg/day of benzene. This was derived using estimates which have varying degrees of support in terms of hard data. The specific use of the total exposure estimates for calculation of water criterion does not seem warranted at this particular time because of a general lack of knowledge about the accuracy of the estimates. It can be said, however, that from a general weight of evidence perspective, it appears that air exposure may contribute the majority of total exposure.

The total exposure consideration should be factored into the criterion development at a later date when additional data is available.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Benzene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of benzene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of benzene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7} (μg/l)	10^{-6} (μg/l)	10^{-5} (μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish.[2]	0	0.15	1.5	15
Consumption of fish and shellfish only.	0	1.5	15	250

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the human epidemiology data presented in the Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentration corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Six percent of the benzene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 6.9 fold. The remaining 94 percent of benzene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of benzene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding benzene concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding benzene concentrations.

Although total exposure information for benzene is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into ambient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

Summary of Pertinent Data

Three epidomiology studies of workers exposed to benzene vapors on their jobs, performed by Infante, Ott, and Askoy, were reviewed by the CAG for the Office of Air Quality Planning and Standards. (Albert, 1978).[1] Their result was that the potency for humans breathing benzene continuously is $B=0.02407$. This means that the lifetime risk of getting leukemia, R, equals 0.024074 times the lifetime average continuous exposure, X, measured as ppm of benzene by volume in air, or $R=BX$. Therefore the air concentration, X, resulting in a risk of 10^{-5} is $X=R/B=10^{-5}/.024074=4.1539\times10^{-4}$ ppm.

Since the air concentration corresponding to 1 ppm of benzene is $3.25\times10^{3}\mu g/m^3$ and since people breathe an average of 24 m^3/day of air, the daily intake that would result in a risk of 10^{-5} is:

$$4.154\times10^{-4}\text{ ppm}\times 3.25\times10^{3}\text{ mg/m}^3\text{ per ppm}\times 24\text{ m}^3/\text{day}=32.4\mu g/\text{day}$$

If it is assumed that the fraction of benzene intake reaching the target site is the same via inhalation and ingestion of water and fish, a daily benzene intake of 32.4 μg through drinking water and fish alone would also cause a leukemia risk of 10^{-5}. The water concentration giving this intake is:

$$C=(32.4\mu g/\text{day})/(2+6.9)(0.0187)$$
$$=15.22\mu g/1$$
$$=15\mu g/1$$

BERYLLIUM

Criteria Summary:

Freshwater Aquatic Life.

For beryllium the criterion to protect freshwater aquatic life as derived using the Guidelines is "$e^{(1.24\cdot1n\ (\text{hardness})-6.65)}$" as the 24-hour average concentration (see the figure "24-hour average beryllium concentration vs. hardness") and the concentration should not exceed "$e^{(1.24\cdot1n\ (\text{hardness})-1.46)}$" (see the figure "maximum beryllium concentration vs. hardness") at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for beryllium can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to beryllium through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of beryllium estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formula-

[1] Albert, R. 1978. Carcinogen Assessment Group's final report on the population risk to ambient benzene exposures. September 12, 1978.

tion section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 0.087μg/1, 0.0087μg/1, and 0.00087μg/1, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of beryllium is the Final Acute Value of $e^{(1.24 \cdot \ln(\text{hardness}) - 1.46)}$ and the 24-hour average concentration is the Final Chronic Value of $e^{(1.24 \cdot \ln(\text{hardness}) - 6.65)}$. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For beryllium the criterion to protect freshwater aquatic life as derived using the Guidelines is "$e^{(1.24 \cdot \ln(\text{hardness}) - 6.65)}$" as a 24-hour average and the concentration should not exceed "$e^{(1.24 \cdot \ln(\text{hardness}) - 1.46)}$ at any time.

Summary of Available Data

All concentrations herein are expressed in terms of beryllium.

Final Fish Acute Value=$e^{(1.24 \cdot \ln(\text{hardness}) + 0.55)}$

Final Invertebrate Acute Value=$e^{(1.24 \cdot \ln(\text{hardness}) - 1.46)}$

Final Acute Value=$e^{(1.24 \cdot \ln(\text{hardness}) - 1.46)}$

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=$e^{(1.24 \cdot \ln(\text{hardness}) - 6.65)}$

Final Plant Value=100,000μg/1

Residue Limited Toxicant Concentration=not available

Final Chronic Value=$e^{(1.24 \cdot \ln(\text{hardness}) - 6.65)}$

Saltwater Aquatic Life

No saltwater criterion can be derived for beryllium using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

Reduced alkaline phosphatase activity in the mummichog has been reported. Gross embryonic effects were observed in the sea urchin at a concentration of 9,010 μg/l. No other data on the effects of beryllium on saltwater species are available.

Human Health

Experiments have shown cancer by beryllium can be experimentally produced in laboratory animals. As can be seen in Talbes 1 and 2, cancer has been produced by inhalation, intratracheal instillation, and intravenous injection of beryllium. Beryllium chloride has been shown to increase the error frequency of nucleotide base incorporation into DNA in an *in vitro* assay designed to detect potential metal mutagen/carcinogens. Finally, evidence is accumulating that inhalation of beryllium may cause lung cancer in humans.

Epidemiological studies have failed to establish an incontrovertible link between beryllium exposure and human cancer, and cancer was not produced in one experimental that, 2) we are relying on the Schroeder and Mitchener study because it is the only available data for oral ingestion from which a concentration range can be calculated. To extrapolate from the Be studies where the route of administration was by injection would yield a lower, and, we believe, less valid number for oral ingestion.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Beryllium is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of beryllium in water for maximum protection of human health is ZERO.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of beryllium corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the Table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7} (μg/l)	10^{-6} (μg/l)	10^{-5} (μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish.[2]	0	0.00087	0.0087	0.087
Consumption of fish and shellfish only.	0	0.0056	0.056	0.56

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Appendix I. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1000, and so forth.

[2] 15 percent of the beryllium exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 19 fold. The remaining 85 percent of beryllium exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of beryllium, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding beryllium concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding beryllium concentrations. Because data indicating other sources of beryllium exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Summary of Pertinent Data

Although beryllium was shown to produce bone osteosarcomas at an extremely low dose via intravenous injection, the experiments of Schroeder and Mitchener (1975)[1] on rats and mice at 5 ppm in drinking water induced no observed carcinogenic response, except for a small statistically insignificant excess rate of "lymphoma leukemias" in female mice and in grossly observed tumors of all sites in male rats. The small absorption from the gastrointestinal tract is presumably the reason for the lack of significant effect. If beryllium is carcinogenic via ingestion it must be less potent than observed by Schroeder and Mitchener. Therefore, that experiment can be used to estimate the maximum risk that beryllium could pose, or equivalently, the lowest concentration which leads to a 10^{-5} lifetime risk.

In the male rats given 5 ppm in the drinking water, nine out of 33 treated animals had grossly observed tumors of some type, whereas four out of 26 controls had tumors. With a bioaccumulation factor of 1.0, the parameters of the extrapolation model are:

$n_t=9$
$N_t=33$
$n_c=4$
$N_c=26$
$Le=1126$ days
$le=1126$ days
$d=5$ ppm$\times 0.05=0.25$ mg/kg/day
$L=1126$ days
$w=0.385$ kg
$R=19.0$

The result is that the water concentration does not need to get any lower than 0.087 micrograms per liter in order to keep the lifetime risk below 10^{-5}.

CADMIUM

Criteria Summary:

Freshwater Aquatic Life

For cadmium the criterion to protect freshwater aquatic life as derived using the Guidelines is e(0.87 ln (hardness)−4.38) as a 24-hour average. Cadmium concentration should not exceed e(1.30 ln (hardness)−3.92) at any time.

Saltwater Aquatic Life

For cadmium the criterion to protect saltwater aquatic life as derived using the Guidelines is 1.0 μg/l as a 24-hour average and the concentration should not exceed 16 μg/l at any time.

Human Health

For the protection of human health from the toxic properties of cadmium ingested through water and through contaminated aquatic organisms, the ambient water criterion is determined to be 10μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of cadmium is the Final Acute Value of e(1.30·ln(hardness)−3.92) and the 24-hour average concentration is the Final Chronic Value of e(0.867·ln(hardness)−4.38). No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For cadmium the criterion to protect freshwater aquatic life as derived using the Guidelines is "e(.867·ln(hardness)−4.38)" as a 24-hour average (see the figure "24-hour average cadmium concentration vs. hardness") and the concentration should not exceed "e(1.30·ln(hardness)−3.92)" (see the figure "maximum cadmium concentration vs. hardness") at any time.

Summary of Available Data

Final Fish Acute Value=e(1.30·ln(hardness)−3.92)
Final Invertebrate Acute Value=e(1.30·ln(hardness)−1.57
Final Acute=e(1.30·(hardness)−3.92
Final Fish Chronic Value=e(0.867·ln(hardness)−3.70)
Final Invertebrate Chronic Value=e(0.867·ln(hardness)−4.38)
Final Chronic Value=(0.867·ln (hardness)−4.38)
Final Plant Value=2μg/l
Residue Limited Toxicant Concentration=39μg/l

Saltwater Aquatic Life

The maximum concentration of cadmium is the Final Acute Value of 16μg/l and the 24-hour average concentration is the Final Chronic Value of 1.0μg/l. No important adverse effects on saltwater organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For cadmium the criterion to protect saltwater aquatic life as derived using the Guidelines is 1.0μg/l as a 24-hour average and the concentration should not exceed 16μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of cadmium.

Final Fish Acute Value=3,000μg/l
Final Invertebrate Acute Value=16μg/l
Final Acute Value=16μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=1.0μg/l
Final Plant Value=160μg/l
Residue Limited Toxicant Concentration=140μg/l
Final Chronic Value=I.0μg/l
0.44×Final Acute Value=7.0μg/l

Human Health

There is no doubt that cadmium is a teratogen in several rodent species when given in large parenteral doses. Doses of this magnitude (4-12 mg/Kg) would surely produce severe, if not fatal toxic symptoms in man. In the human only small amounts of cadmium cross the placental barrier.

Only one report, from Russia suggests any effect, i.e. low birth weight and "several children with rickets or dental trouble." Details are lacking in this report and it should not be construed as implicating cadmium without further data.

The studies of whether cadmium is mutagenic are inconsistent. The reports of chromosomal aberrations in both Itai-Itai patients and cadmium workers are conflicting. Dominant lethal studies have been negative as are tests for spermatocytic chromosome aberrations in male mice and their first-generation offspring. Studies of mutagenic activity in non-mammalian life forms have given inconsistent results.

There is no question that the injection of cadmium into rodents results in injection-site sarcomas and interstitial cell tumors of the testis. Sarcoma production in rats is a common sequela to the injection of irritants and could be regarded as a non-specific response to fibroblast injury. Interstitial tumors apear to result from the hy-

[1] Schroeder, H. A., and M. Mitchener. 1975. Life-term studies in rats: Effects of aluminum, barium, beryllium, and tungsten. Jour. Nutr. 105:420.

perplasia and metaplasia of tissue regeneration following vascular mediated testicular damage. There is no evidence that these tumors are malignant neoplasms, however, this does not refute the tumorogenic potential of cadmium.

The human evidence for the carcinogenicity of cadmium is conjectural, based on very small numbers, and confounded by exposures to other elements which are known to be human carcinogens. The reports on British battery workers and the work of Lemen, et al. suggest an increase in prostrate and lung cancer. These men were also exposed to nickel and/or arsenic, but in amounts of 1/100's-2/200's of cadmium exposure level. Kolonel's work confirmed neither of these sites, but suggested an association with renal cancer. This work is inadequate in that it assures an exposure to cadmium based upon an occupational questionnaire. There have been *no* case reports of renal cancer in known cadmium-exposed workers. Cigarette smoking would appear to have a firmer association with renal neoplasia, rather than cadium. The geographic distribution of prostate cancer (Japan, Sweden, USA) suggests that an *inverse* relationship exists to cadmium exposure. From the known mortality study data cited it might be argued that cadmium exposure reduces general mortality or is a potent protective factor against cardiovascular disease. The case for cadmium as a carcinogen is not persuasive when the existing data are critically reviewed, but it has been viewed by some as suggestive from the public health perspective.

It is not recommended that cadmium be considered a suspect human carcinogen for purposes of calculating a water quality criterion. However, the weight of evidence for oncogenic potential of cadmium is sufficient to be "qualitatively suggestive" and is not to be ignored from a public health point of view. The EPA Carcinogen Assessment Group has reviewed cadmium and their summary is included in the Appendices of this document.

The criterion is based on established health effects. The data implicating cadmium as a cause of emphysema and renal tubular proteinuria is firmly established. Emphysema has been reported only after airborne exposures and has been documented for both man and animals. It would seem to result from a direct effect upon lung tissue of which cadmium salts are known irritants.

There is evidence from occupational studies that the kidney is more sensitive to the effects of cadmium than the lung. In exposed workers proteinuria occurs in higher incidence and in a shorter time period than emphysema. It seems entirely justified to conclude that the kidney is the critical target organ.

It is generally accepted that the critical cadmium level at which renal dysfunction occurs is approximately 200 $\mu g/g$ wet weight of renal cortex. Autopsy studies indicate that at present the average kidney concentration in non-smokers is approximately one-twelfth this level. In smokers the concentration is about twice as high, i.e. 30–39$\mu g/g$.

Friberg has estimated that the critical level is reached at daily ingestion levels of 250–350μg per day over 50 years. Since the average, non-occupationally exposed American probably does not have an intake from all sources exceeding 25–50μg there would again seem to be a reasonable "safety-factor" of 5 to 12 in existence. While this is not the comfortable margin or many orders of magnitude usually recommended by toxicologists it should provide a margin of "safety" to the general public for the foreseeable future.

NIOSH recommends that workers should not be exposed to airborne cadmium at a concentration greater than 40$\mu g/m^3$ as a time weighted exposure for up to a 40 hour work week. This standard is designed to protect the health and safety of workers over an entire working life time. Compliance should prevent adverse effects on the health of the worker. Several studies have indicated no adverse effects at levels of 31 and 16–29$\mu g/m^3$.

Effects of renal function (proteinuria) and a reduction in mean pulmonary function have been noted at levels of 66$\mu g/m^3$ although some of these workers probably had experienced exposure, at least intermittently to cadmium fur at higher, but unkown concentrations. The limit of 40$\mu g/m^3$ offers a greater, and "probably sufficient margin of safety, in comparison with the 50$\mu g/m^3$ recommended by ACGIH and Lauwerys, et al.

From the figure 40$\mu g/m^3$ it can be calculated that a worker might absorb about a 1000 μg during a work week, i.e. 40$\mu g/m^3 \times 10 m^3$ inhaled/day 5 days 0.5 (lung absorption rate). This is approximately 286μg/day intake and 143μg/day absorbed. To this the average daily intake from food and general environmental sources can be added, i.e. 10–50μg. This suggests that an exposed worker may have an approximate intake of 300 μg/d and still be safe. However, a healthy worker may not be representative of the American population as a whole.

From Japanese dietary intake data where Itai-Itai disease is prevalent, and studies on the age-specific incidence of proteinuria, it is possible to estimate a no-effect level for ingested cadmium. In areas where Itai-Itai disease is most common, about 85 percent of the daily cadmium intake is derived from rice, the locally grown grain staple.

Nogawa, et al. have shown that the prevalence of tubular proteinuria, as measured by retinol binding protein excretion, in persons under age 70 does not begin to rise above that seen in control populations until the cadmium levels in rice exceed 0.40–0.49μg/gm. The Japanese diet in the area of endemic Itai-Itai disease and even in the homes of patients with the disease are precisely known.

Approximately 2100 calories are consumed daily, with carbohydrate accounting for about 1725 calories daily, which is equivalent to the ingestion of 430 gm/d. The no-effect level for Japanese can be calculated as follows:

$$\frac{430 \text{ gm/d.} \times 0.45\mu g/\text{gm (rice)} = 228\mu g/\text{day}}{0.85}$$

This Japanese figure is slightly below the estimate of 250μg/day given by Friberg as an effect level. The no-effect level for a western European or American population with correspondingly larger body size would be expected to be somewhat greater (i.e., 301μg/day).

The Working Group of Experts for the Commission of European Communities has estimated that the threshold effect level of cadmium by ingestion at around 200μg daily corresponding to an actual absorption of 12μg/day. For smokers this estimate is reduced by about 1.0μg to 10.1μg which corresponds to an oral intake of 169μg. Using a second approach based on metabolic modeling of the above type, this same group derived a threshold effect level of 248μg daily when pulmonary absorption is negligible.

Using the data presented in this and preceeding sections of the document, it is possible to construct several exposure scenarios encompassing possible best-to-worse case exposure situations that might be domestically encountered:

WORST CASE—MAXIMALLY EXPOSED PERSONS

Exposure sources	Exposure	Cd intake/d (μg)	Absorption factor*	Cd retention/d (μg)
Air-Occupational	*0.1 mg/m³	714.0	0.8	357.0
Air-Ambient	400 μg/m³	8.0	0.5	4.0
Air-Smoking (three packs)	3.0 μg/pack	9.0	0.5	4.5
Foods		**75.0	0.1	7.5
Drinking Water	***10 μg/l	20.0	0.1	2.0
Total		826.0		375.0

AVERAGE CASE

Air-Ambient	0.03 μg/m³	0.60	0.25	0.150
Air-Smoking (one pack)	3.0 μg/pack	3.00	0.25	0.750
Food		30.00	0.05	1.500
Drinking Water	1.3 μg/l	2.60	0.05	0.130
Total		36.20		2.530

BEST CASE—MINIMALLY EXPOSED PERSONS

Air-Ambient	0.001 μg/m³	0.02	0.25	0.005
Food		12.00	0.05	0.600
Water	*0.5 μg/l	1.00	0.05	0.050
Total		13.02		0.655

* Average for both sexes excluding drinking water.
* These absorption factors are considered to be the most realistic available.

From these scenarios it can be calculated that ingested water contributes relatively little to the daily retained cadmium entering the body i.e., 0.53, 5.1, and 7.6 percent respectively for the worst, average, and best cases. Water could become a significant contributor to all over cadmium intake and retention only if the scenarios are reconstructed by substituting the worst case water data for that in the average and best cases. However, even in the very unlikely event that such situations occur the total cadmium intake and retention remain comparatively modest i.e., 53.6μg/d intake and 4.4μg/d retained in the average case. The totals for the best case substitution are substantially less i.e., 32.02 μg/d intake and 2.605μg/d retention. Therefore, it may be concluded that there are no circumstances in which ambient waters meeting current drinking water standards pose a threat to human health.

Based on the foregoing data and discussion it seems entirely justifiable to conclude that water constitutes only a relatively minor portion of man's daily cadmium intake. From the above analysis it is obvious (average case scenario) that drinking water contributes substantially less to human cadmium intake and/or retention than smoking a package of cigarettes daily. From this analysis it appears that a water criterion needs to be more stringent than the existing Primary Drinking Water Standard (10μg/l) to provide ample protection of human health.

CARBON TETRACHLORIDE

Criteria Summary:

Freshwater Aquatic Life

For carbon tetrachloride, the criterion to protect freshwater aquatic life, as derived using procedures other than the guidelines, is 620μg/l as a 24-hour average and the concentration should never exceed 1,400μg/l at any time.

Saltwater Aquatic Life

For carbon tetrachloride, the criterion to protect saltwater aquatic life, as derived using procedures other than guidelines, is 2,000μg/l as a 24-hour average and the concentration should never exceed 4,600μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to carbon tetrachloride through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of carbon tetrachloride estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 2.6μg/l, 0.26μg/l, and 0.026μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for carbon tetrachloride using the Guidelines because no Final Chronic Value for either fish or invertebrates or a good substitute for either value is available.

However, results obtained with structurally similar compounds indicate how a criterion may be estimated.

The Final Chronic Value for chloroform and freshwater organisms, based on an invertebrate species, is about the same as 0.44 times the Final Acute Value. The Final Chronic Value for bromoform and saltwater organisms, based on a fish species, is greater than 0.44 times the Final Acute Value. Therefore, it seems reasonable to estimate a criterion for carbon tetrachloride and freshwater organisms using 0.44 times the Final Acute Value.

To estimate a criterion for carbon tetrachloride, the maximum concentration is the Final Acute Value of 1,400μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For carbon tetrachloride, the criterion to protect freshwater aquatic life, as derived using procedures othe than the Guidelines, is 620μg/l as a 24-hour average and the concentration should never exceed 1,400μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=8,200μg/l

Final Invertebrate Acute Value =1,400μg/l

Final Acute Value=1,400μg/l

Final Fish Chronic Value=greater than 250μg/l

Final Invertebrate Chronic Value =not available

Final Plant Value=not available

Residue Limited Toxicant Concentration=not available

Final Chronic Value=greater than 250μg/l

0.44×Final Value=620μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for carbon tetrachloride using the Guidelines because no Final Chronic Value for either fish or invertebrates or a good substitute for either value is available.

However, results obtained with carbon tetrachloride and structurally similar compounds with freshwater and saltwater organisms indicate how a criterion may be derived.

The Final Invertebrate Acute Value divided by the Final Fish Acute Value for bromoform and methylene chloride with freshwater and saltwater organisms and for chloroform and carbon tetrachloride with freshwater organisms is 0.46, 0.29, 0.16, 0.090, 0.11, and 0.17 respectively, for an average of 0.21. When this is multiplied by the Final Acute Value for carbon tetrachloride and saltwater fish, an estimated Final Invertebrate Acute Value of 0.21×22,000μg/l=4,600μg/l is obtained. Thus the Final Acute Value for carbon tetrachloride is 4,600μg/l.

The Final Chronic Value for chloroform and freshwater organisms is about the same as 0.44 times the Final Acute Value, and the Final Chronic Value for bromoform and saltwater organisms is greater than 0.44 times the Final Acute Value, even though a chronic value is available for fish or invertebrate species in both cases. Therefore, it seems reasonable to estimate a criterion for carbon tetrachloride and saltwater organisms using 0.44 times the Final Acute Value which for carbon tetracholoride is 2,000μg/l.

To estimate a criterion for carbon tetrachloride, the maximum concentration is the Final Actue Value of 4,600μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For carbon tetrachloride, the criterion to protect saltwater aquatic life, as derived using procedures other than the Guildelines, is 2,000μg/l as a 24-hour average and the concentration should never exceed 4,600μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=22,000μg/l

Final Invertebrate Acute Value=not available

Final Acute Value=22,000μg/l

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value =not available

Final Plant Value=not available

Residue Limited Toxicant Concentration=not available

Final Chronic Value=not available

0.44×Final Acute Value=9,700μg/l

Human Health

Studies indicate that CCl_4 has a full spectrum of toxic effects. Historically, industral and accidental exposures to CCl_4 by ingestion, inhalation and dermal routes have produced acute, subacute and chronic poisoning with fatalities. Generally speaking, acute toxicity for both man and animals can be characterized as nodular hyperplasia and cirrhosis of the liver and renal dysfunction. Mutagenic effects have not been observed and teratogenic effects have not been conclusively demonstrated.

The most significant effect to consider in terms of dose/response is the cancer causing potential of the chemical. Current knowledge leads to the conslusion that carcinogenesis is a non-threshold, non-reversible process. The non-threshold concept implies that many tumors will be produced at high doses, but any dose, no matter how small, will have the probability of causing cancer. Even small carcinogenic risks have a serious impact on society when the exposed population is large, because it is likely that some cancers will be caused by exposure to CCl_4. The nonreversible concept implies that once the tumor growth process has started, growth will continue and may metastasize and involve other organs until death ensues.

There is a sufficient weight of evidence to conclude that CCl_4 is a carcinogen in laboratory animals and with appropriate assumptions is interpreted to be a suspect human carcinogen.

Under the Consent Decree in NRDC vs. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Carbon tetrachloride is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the appropriate concentration of carbon tetrachloride in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of carbon tetrachloride corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish.[2]	0	0.020	0.26	2.6
Consumption of fish and shellfish only	0	0.067	0.67	6.7

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately 39 percent of the carbon tetrachloride exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 69 fold. The remaining 61 percent of carbon tetrachloride exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of carbon tetrachloride (1) occurring from consumption of both drinking water and aquatic life grown in waters containing the corresponding carbon tetrachloride concentrations and (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding carbon tetrachloride concentrations. Although total exposure information for carbon tetrachloride is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into ambient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

CHLORDANE

Criteria Summary:

Freshwater Aquatic Life

For chlordane the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.024μg/l as a 24-hour average and the concentration should not exceed 0.36μg/l at any time.

Saltwater Aquatic Life

For chlordane the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0091μg/l as a 24-hour average and the concentration should not exceed 0.18μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to chlordane through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of chlordane estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 1.2 μg/l, 0.12 μg/l, and 0.012 μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of chlordane is the Final Acute Value of 0.36μg/l and the 24-hour average concentration is the Final Chronic Value of 0.024μg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For chlordane the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.024μg/l as a 24-hour average and the concentration should not exceed 0.36μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=16μg/l

Final Invertebrate Acute Value=0.36μg/l

Final Acute Value=0.36μg/l

Final Fish Chronic Value=0.24μg/l

Final Invertebrate Chronic Value=3.2μg/l

Final Plant Value=not available

Residue Limited Toxicant Concentration=0.024μg/l

Final Chronic Value=0.024μg/l

0.44×Final Acute Value=0.16μg/l

Saltwater Aquatic Life

The maxium concentration of chlordane is the Final Acute Value of 0.18μg/l and the 24-hour average concentration is the Final Chronic Value of 0.0091μg/l. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For chlordane the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0091μg/l as a 24-hour average and the concentration should not exceed 0.18μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=3.2μg/l

Final Invertebrate Acute Value=0.18μg/l

Final Acute Value=0.18μg/l

Final Fish Chronic Value=0.28μg/l

Final Invertebrate Chronic Value=not available

Final Plant Value=1,000μg/l

Residue Limited Toxicant Concentration=0.0091μg/l

Final Chronic Value=0.0091μg/l

0.44 × Final Acute Value=0.79μg/l

Human Health

Several approaches are available to estimate a criterion level for chlordane in ambient water. Using the Food and Agricultural Organization/World Health Organization value of 0.001 mg/kg of body weight as the maxium daily human intake, and assuming an average body weight of 70 kg, the allowable intake would be 70μg/day. Further, subtracting Nisbet's value of 9μg as the daily intake from fish, shellfish, milk, inhalation, etc., and assuming that the contribution from drinking water is a negligible part of this value, the ambient water criterion becomes 61μg/day. At 2 liters per day consumption, the maximum allowable concentration would be 30μg/l.

The proposed U.S. EPA drinking water regulations the Canadian standards, and the National Technical Advi-

sory Committee all suggest a chlordane limit of 3μg/l for drinking water. The latter report specifically indicates that the water treatment process has little effect on chlordane.

Although there are limitations to the procedure, the industrial inhalation exposure limit of the American Conference of Governmental Industrial Hygienists may be converted to a limit for ingestion. Assuming absorption via the GI tract for chlordane is one-fifth the absorption by inhalation:

$$0.5\ \text{mg} \times 10\text{m}^3\text{T1} \times 5\text{d work week} \times 1 = 0.7\ \text{mg/day}$$

$$\text{m}^3 \quad \text{workday} \quad \text{7d week} \quad 5$$

Consumption of 2 liters of water daily and the consumption of 18.7 grams of contaminated fish which have a bioconcentration factor of 5,500 result in a maximum permissible concentration of 6.7μg/l for the ingested water.

The use of inhalation data assumes an 8-hour day, time-weighted average occupational exposure in the working place with workers inhaling the toxic substance throughout such a period. Exposures for the general population should be considerably less. Such worker-exposure inhalation standards are inappropriate for the general population since they presume an exposure limited to an 8-hour day, an age bracket of the population that excludes the very young and the very old, and a healthy worker prior to exposure. Ingestion data is superior to inhalation data when the risks associated with the food and water of the water environment are being considered.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities". Chlordane is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of chlordane in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of chlordane corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, $^{-6}$, or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7} (μg/l)	10^{-6} (μg/l)	10^{-5} (μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.011	0.11	1.2
Consumption of fish and shellfish only	0	0.011	0.13	1.3

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in the Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] 98 percent of the chlordane exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 5,500-fold. The remaining 2 percent of chlordane exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of chlordane, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding chlordane concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding chlordane concentrations. Because data indicating other sources of chlordane exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Summary of Pertinent Data

The IRDC lifetime study of chlordane at 25 ppm in the diet of CD-1 mice resulted in liver carcinomas in males in 41 of 52 treated mice and in 3 of 33 controls, according to a re-analysis of slides by Dr. Reuber (CAG report). Using a fish bioconcentration factor of 5,500 the water concentration estimated to result in a lifetime risk of 10^{-5} is calculated from the extrapolation model using the following parameters:

$n_t = 41$
$N_t = 52$
$n_c = 3$
$N_c = 33$
$Le = 78$ weeks
$le = 78$ weeks
$d = 25 \times 10^{-6} \times 0.13 \times 10^{-6}$ mg food per day/kg body weight = 3.25 mg/kg/day
$w = 0.041$ kg
$L = 78$ weeks
$F = 0.0187$ kg
$R = 5{,}500$

The result is that the water concentration corresponding to a lifetime risk of 10^{-5} is 1.2 nanograms/liter.

CHLORINATED NAPHTHALENES

Criteria Summary:

Freshwater Aquatic Life

For 1-chloronaphthalene, the criterion to protect freshwater aquatic life, as derived using procedures other than the Guidelines, is 29μg/l as a 24-hour average and the concentration should never exceed 67μg/l at any time.

Saltwater Aquatic Life

For 1-chloronaphthalene, the criterion to protect saltwater aquatic life, as derived using the Guidelines, is

2.8μg/l as a 24-hour average and the concentration should never exceed 6.4μg/l at any time.

Human Health

For the protection of human health from the toxic properties of chlorinated naphthalenes ingested through water and through contaminated aquatic organisms, the ambient water criteria for the various classes of chlorinated naphthalenes are:

	Criterion level (μg/l)
Trichloronaphthalenes	3.9
Tetrachloronaphthalenes	1.5
Pentachloronaphthalenes	0.39
Hexachloronaphthalenes	0.15
Octachloronaphthalene	0.08

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for any chlorinated naphthalene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

Data for 1-chloronaphthalene and saltwater organisms can be used to estimated a criterion.

For 1-chloronaphthalene and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from results of an embryo-larval test with the sheepshead minnow. Therefore, a reasonable estimate of a criterion for 1-chloronaphthalene and freshwater organisms would be 0.44 times the Final Acute Value.

The maximum concentration for 1-chloronaphthalene is the Final Acute Value of 67μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1-chloronaphthalene the criterion to protect freshwater aquatic life as drived using procedures other than the Guidelines is 29μg/l as a 24-hour average and the concentration should not exceed 67μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1-chloronaphthalene

Final Fish Acute Value=320μg/l
Final Invertebrate Acute Value=67μg/l
Final Acute Value=67μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=1,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=1,000μg/l
0.44 × Final Acute Value=29μg/l

Saltwater Aquatic Life

The commercial mixtures of chlorinated naphthalenes are not considered in the development of a criterion since the toxicity of each chlorinated naphthalene in the mixtures may be different, and different proportions of these individual chemicals would have different toxicity.

The maximum concentration of 1-chloronaphthalene is the Final Acute Value of 6.4μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1-chloronaphthalene the criterion to protect saltwater aquatic life as derived using the Guidelines is 2.8μg/l as a 24-hour average and the concentration should not exceed 6.4μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1-chloronaphthalene

Final Fish Acute Value=350μg/l
Final Invertebrate Acute Value=6.4μg/l
Final Acute Value=6.4μg/l
Final Fish Chronic Value=49μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=1,100μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=49μg/l
0.44 × Final Acute Value=2.8μg/l

Human Health

There are insufficient animal toxicity data available on which to base a criterion for polychlorinated naphthalenes. However, industrial exposure to vapors of polychlorinated naphthalenes has resulted in systemic toxicity, and this toxicity is the basis for the present ACGIH [1] threshold limit values (TLV). Such a TLV can be used as a basis for developing water criteria for polychlorinated naphthalenes. It is recognized that the ACGIH TLVs apply primarily to normal adult working males and do not incorporate safety factors for sensitive populations. In order to provide a reasonable margin of safety, calculation of an acceptable concentration of polychlorinated naphthalenes in drinking water as proposed by the Stokinger and Woodward model should include a safety factor of 100 as illustrated below:

$$\frac{\text{TLV (mg/m}^3) \cdot 50\ \text{m}^3/\text{wk}}{7\ \text{days/wk} \cdot 100} = \text{acceptable intake (mg/day)}$$

where

50 m^3/wk=average amount of air inhaled by a normal adult in a 40 hour work week;
7 days/wk=conversion factor for daily intake;
100=safety factor for sensitive populations.

Since no pharmacokinetic data are available to compare absorption efficiency by the inhalation route versus the oral route, it is assumed that absorption efficiency is the same by either route.

Using the ACGIH TLV levels, the acceptable daily intakes for polychlorinated naphthalenes would be as follows:

	Acceptable daily intake (mg)
Trichloronapthalenes	0.36
Tetrachloronaphthalenes	0.14
Pentachloronaphthalenes	0.036
Hexachloronaphthalenes	0.014
Octachloronaphthalene	0.007

Assuming an average intake of 18.7 g of fish per day with a biomagnification factor of 4,800 for edible portions of aquatic species as derived in the Exposure section, and a water intake of 2 l/day, then criteria levels for the above polychlorinated naphthalenes in water would be as follows:

	Criterion level (μg/l)
Trichloronaphthalenes	5.9
Tetrachloronaphthalenes	1.5
Pentachloronaphthalenes	0.39
Hexachloronaphthalenes	0.15
Octachloronaphthalene	0.08

CHLOROFORM

Criteria Summary:

Freshwater Aquatic Life

For chloroform, the criterion to protect freshwater aquatic life, as derived using the Guidelines, is 500μg/l as a 24-hour average and the concentration should never exceed 1,200μg/l at any time.

[1] American Conference of Governmental Industrial Hygienists. 1977. TLVs Threshold Limit Values for chemcial substances and physical agents in the workroom environment with intended changes. Cincinnati, Ohio.

Saltwater Aquatic Life

For chloroform, the criterion to protect saltwater aquatic life, as derived using procedures other than the Guidelines, is 620μg/l as a 24-hour average and the concentration should never exceed 1,400μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to chloroform through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of chloroform estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 2.1μg/l, 0.21μg/l, and 0.021μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of chloroform is the Final Acute Value of 1,200μg/l and the 24-hour average concentration is the Final Chronic Value of 500μg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For chloroform the criterion to protect freshwater aquatic life as derived using the Guidelines is 500μg/l as a 24-hour average and the concentration should not exceed 1,200μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=11,000μg/l
Fish Invertebrate Acute Value=1,200μg/l
Final Acute Value=1,200μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=500μg/l
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=500μg/l
0.44× Final Acute Value=530μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for chloroform using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

Results obtained for chloroform with freshwater organisms and for structurally similar compounds with both freshwater and saltwater organisms provide an alternate method to estimate a criterion.

With freshwater organisms the Final Chronic Value derived from data for *Daphnia magna* for chloroform is about the same as 0.44 times the Final Acute Value; and with saltwater organisms the Final Chronic Value for structurally similar bromoform is greater than 0.44 times the Final Acute Value. Therefore, 0.44 times the Final Acute Value is the best estimate of the 24-hour average concentration.

In regard to acute toxicity, freshwater fish are less sensitive than invertebrates species based upon the Final Fish and Final Invertebrate Acute Values. The same is true for two other halomethanes—bromoform and methylene chloride. For freshwater organisms and carbon tetrachloride, a similar relationship exists. Therefore, the absence of acute data for fish is not constraining and the Final Invertebrate Acute value of 1,400μg/l is used as an estimate for the Final Acute Value. Furthermore, 0.44 times the Final Acute Value is 620μg/l, which becomes an estimate of the criterion for the 24-hour average concentration.

For chloroform the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 620μg/l as a 24-hour average and the concentration should not exceed 1,400μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=not available
Final Invertebrate Acute Value=1,400μg/l
Final Acute Value=1,400μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=not available
0.44×Final Acute Value=620μg/l

Human Health

Chloroform has several adverse effects on the human body. Safe levels of chloroform in water necessary to avoid some of these effects would be difficult to establish because adequate studies have not been conducted. The most serious effect to consider is the cancer-causing potential of the chemical. Current knowledge leads to the conclusion that carcinogenesis is a non-threshold, nonreversible process. The non-threshold concept implies that many tumors will be produced at high doses, but any dose, no matter how small, will have the probability of causing cancer. Even small carcinogenic risks have a serious impact on society when the exposed population is large, because it is likely that some cancers will be caused by chloroform. The nonreversible concept implies that once the tumor growth process has started, growth will continue and may metastasize and involve other organs until death ensues.

Chloroform has been shown to induce cancer in two species of experimental animals. This conclusion is neither confirmed nor denied by the results of numerous epidemiology studies now available although from a public health point of view, a suspicion of a qualitative weight of evidence for confirmation probably exists.

The available information on total human exposure to chloroform from air, water and food sources suggests that drinking water contributes from 6 percent to 69 percent of the total exposure. Considering that chloroform levels in drinking water are enhanced by water treatment processes on the one hand and that chloroform levels in waste discharges may be similarly enhanced by waste treatment processes, it is difficult to utilize the total exposure information in formulating an ambient water quality criterion, except to say that exposure through water is likely to be more significant than other exposure routes.

It is therefore proposed that the total risk for carcinogenic response be allocated to the ambient water exposure conditions of ingesting 2 liters/day of water and consuming 18.7 grams of potentially contaminated fish products.

Under the Consent Decree in *NRDC vs. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Chloroform is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of chloroform in water for maximum portection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of chloroform corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people ex-

posed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.021	0.21	2.1
Consumption of fish and shellfish only	0	0.175	1.75	17.5

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1000, and so forth.

[2] Approximately 12 percent of the chloroform exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration of 14 fold. The remaining 88 percent of chloroform exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of chloroform, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding chloroform concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding chloroform concentrations. Although total exposure information for chloroform is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into ambient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

Summary of Pertinent Data

The NCI (1976)[1] bioassay with female mice given a time-weighted average dose of 238 mg/kg of chloroform by stomach tube for 5 times per week for 78 weeks is used for the water quality criterion. The treatment induced hepatocellular carcinomas in 36 of 45 animals examined, whereas the pooled control group had one animal with hepatocellular carcinoma out of 80 animals examined. Assuming a fish bioaccumulation factor of 14, the parameters of the extrapolation model are:

$n_t=36$
$NT=45$
$nc=1$
$NC=80$
$Le=92$ weeks
$le=78$ weeks
$d=238\times5/7=170$ mg/kg/day
$w=0.030$ kg
$L=92$ weeks
$R=14$
$F=.0187$ kg

The result is that the water concentration should be less than 2.1μg/l in order to keep the individual lifetime risk below 10^{-5}.

2-CHLOROPHENOL

Criteria Summary:

Freshwater Aquatic Life

For 2-chlorophenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 60μg/l as a 24-hour average and the concentration should not exceed 180μg/l at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for 2-chlorophenol can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the prevention of adverse effects due to the organoleptic properties of 2-Chlorophenol in water, the criteria is 0.3μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of 2-chlorophenol is the Final Acute Value of 180μg/l and the 24-hour average concentration is the Final Chronic Value of 60μg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 2-chlorophenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 60μg/l as a 24-hour average and the concentration should not exceed 180μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=1,800μg/l
Final Invertebrate Acute Value=180μg/l
Final Acute Value=180μg/l
Final Fish Chronic Value=greater than 290μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=500,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=60μg/l for tainting of fish flesh
0.44×Final Acute Value=79μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for 2-chlorophenol using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

None available.

Human Health

Insufficient data exists to indicate that 2-chlorophenol is a carcinogenic agent. Only one study was designed to detect the promoting activity of 2-chlorophenol with dimethylbenzanthracene initiated tumors. Although carcinogenic promoters may pose a possible carcinogenic risk to man there are no dose/response data on which to base a qualitative risk extrapolation. (Under certain environmental conditions, 2-chlorophenol may produce a small amount of dibenzo-p-dioxin, which is an unsubstituted analog of chlorinated dibenzo-p-dioxins. The recent NCI bioassay report of possible carcinogenicity of dibenzo-p-dioxin has concluded that dibenzo-p-dioxin was not carcinogenic for Osborne-Mendel rats or B6C3F1 mice.) In fact, insufficient health effects data exists on any chronic or acute effect of 2-chlorophenol. In view of this, the recommended criterion is based on organoleptic effects.

The data of investigations evaluating the odor of 2-chlorophenol in drinking water indicate that a low concentration is capable of causing discern-able odor. None of these studies indicate if the threshold odor concen-

[1] National Cancer Institute. 1976. Report on carcinogenesis bioassay of chloroform. Natl. Tech. Inf. Serv. PB-264018. Springfield, Va.

tration made the water unacceptable for consumption. These studies coupled with flavor impairment studies suggest that the selection of 0.3μg/l 2-chlorophenol would be sufficient for the prevention of adverse organoleptic effects in water. It should be emphasized that this is a criterion based on aesthetic rather than health effects. Data on human health effects needs to be developed as a more substantial basis for setting a criterion for the protection of human health.

Thus, based on the prevention of adverse organoleptic effects, the interim criterion recommended for 2-chlorophenol is 0.3μg/l.

DICHLOROBENZENES

Criteria Summary:

Freshwater Aquatic Life

For 1,2-dichlorobenzene the criterion to protect freshwater aquatic life as derived using the Guidelines is 44μg/l as a 24-hour average and the concentration should not exceed 99μg/l at any time.

For 1,3-dichlorobenzene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 310μg/l as a 24-hour average and the concentration should not exceed 700μg/l at any time.

For 1,4-dichlorobenzene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 190μg/l as a 24-hour average and the concentration should not exceed 440μg/l at any time.

Saltwater Aquatic Life

For 1,2-dichlorobenzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 15μg/l as a 24-hour average and the concentration should not exceed 34μg/l at any time.

For 1,3-dichlorobenzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 22μg/l as a 24-hour average and the concentration should not exceed 49μg/l at any time.

For 1,4-dichlorobenzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 15μg/l as a 24-hour average and the concentration should not exceed 34μg/l at any time.

Human Health

For the protection of human health from the toxic properties of dichlorobenzene ingested through water and through contaminated aquatic organisms, the ambient water criterion is determined to be 230μg/l total dichlorobenzene (all isomers combined).

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of 1,2-dichlorobenzene is the Final Acute Value of 99μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effect on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,2-dichlorobenzene the criterion to protect freshwater aquatic life as derived using the Guidelines is 44μg/l as a 24-hour average and the concentration should never exceed 99μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1,2-dichlorobenzene

Final Fish Acute Value=1,700μg/l
Final Invertebrate Acute Value=99μg/l
Final Acute Value=99μg/l
Final Fish Chronic Value=150μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=92,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=150μg/l
0.44 x Final Acute Value=44

No freshwater criterion can be derived for either 1,3-dichlorobenzene or 1,4-dichlorobenzene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available for either compound.

However, results obtained with 1,2-dichlorobenzene and freshwater organisms indicate how criteria for other dichlorobenzenes may be estimated.

The Final Chronic Value for 1,2-dichlorobenzene and freshwater organisms is greater than 0.44 times the Final Acute Value, even though a chronic value is available for fish. Therefore, it seems reasonable to estimate criteria for other dichlorobenzenes and freshwater organisms using 0.44 times the Final Acute Value.

To estimate a criterion for 1,3-dichlorobenzene, the maximum concentration is the Final Acute Value of 700 μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,3-dichlorobenzene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 310μg/l as a 24-hour average and the concentration should never exceed 700μg/l at any time.

Summary of Available Data

1,3-dichlorobenzene

Final Fish Acute Value=700μg/l
Final Invertebrate Acute Value=1,100μg/l
Final Acute Value=700μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=150,000 μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=150,000μg/l
0.44 × Final Acute Value=310μg/l

To estimate a criterion for 1,4-dichlorobenzene, the maximum concentration is the Final Acute Value of 440μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,4-dichlorobenzene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 190μg/l as a 24-hour average and the concentration should never exceed 440μg/l at any time.

Summary of Available Data

1,4-dichlorobenzene

Final Fish Acute Value=600μg/l
Final Invertebrate Acute Value=440μg/l
Final Acute Value=440μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=97,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=97,000μg/l
0.44 × Final Acute Value=190μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for any dichlorobenzene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, results obtained with 1,2-dichlorobenzene and freshwater organisms indicate how criteria may be estimated for the dichlorobenzenes.

The Final Chronic Value for 1,2-dichlorobenzene and freshwater organisms is greater than 0.44 times the Final Acute Value, even though a chronic value is available for fish. Therefore, it seems reasonable to estimate criteria for dichlorobenzenes and saltwater organisms using 0.44 times the Final Acute Value.

To estimate a criterion for 1,2-dichlorobenzene, the maximum concentration is the Final Acute Value of 34μg/l

and the 24-hour average concentration is 0.44 times the Final Acute Value. no important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,2-dichlorobenzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 15μg/1 as a 24-hour average and the concentration should never exceed 34μg/1 at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1,2-dichlorobenzene

Final Fish Acute Value=1,200μg/1
Final Invertebrate Acute Value=34μg/1
Final Acute Value=34μg/1
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=44,000μg/1
Residue Limited Toxicant Concentration=not available
Final Chronic Value=44,000μg/1
0.44 × Final Acute Value=15μg/1

To estimate a criterion for 1,3-dichlorobenzene, the maximum concentration is the Final Acute Value of 49μg/1 and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,3-dichlorobenzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 22μg/1 as a 24-hour average and the concentration should never exceed 49μg/1 at any time.

Summary of Available Data

1,3-dichlorobenzene

Final Fish Acute Value=1,100μg/1
Final Invertebrate Acute Value=49μg/1
Final Acute Value=49μg/1
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=50,000μg/1
Residue Limited Toxicant Concentration=not available
Final Chronic Value=50,000μg/1
0.44 × Final Acute Value=22μg/1

To estimate a criterion for 1,4-dichlorobenzene, the maximum concentration is the Final Acute Value of 34μg/1 and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,4-dichlorobenzene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines in 15μg/1 as a 24-hour average and the concentration should never exceed 34μg/1 at any time.

Summary of Available Data

1,4-dichlorobenzene

Final Fish Acute Value=1,100μg/1
Final Invertebrate Acute Value=34μg/1
Final Acute Value=34μg/1
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=55,000μg/1
Residue Limited Toxicant Concentration=not available
Final Chronic Value=55,000μg/1
0.44×Final Acute Value=15μg/1

Human Health

There was not a sufficient weight of evidence from human or animal tests to qualitatively suggest that DCB's are carcinogentic or mutagenic in mammals or to derive a quantitative estimate of acceptable daily intake using cancer risk extrapolation methods. In addition, there were no human data to allow an estimation of the maximum daily oral dose producing no detected adverse effect.

The most usable controlled experimental data on chronic enteric exposure in multiple animal species is that of Hollingsworth, *et al.*

The maximum tested dose level producing no detectable adverse effects in these tests was 18.8 mg/kg/day over a period of six to seven months, for both 1,2-DCB and 1,4-DCB. Assuming the average weight of adult humans to be 70 kg, the average daily intake of water for man to be two liters, the ingestion of 18.7 grams of fish, a fish bioconcentration factor of 200, and applying an uncertainty factor of 1000, the acceptable daily intake (ADI) of 1,2- or 1,4-DCB in man is calculated to be 1.316 mg/day

$$\frac{(ADI=18.8\times 70=1.316).}{1000}$$

The corresponding no adverse effect ambient level in water would be 0.23 mg/l (1.316=x [2+200 (0.0187)]). The similarity of toxicities among he DCB isomers indicates the applicability of this value to 1,3-DCB as well.

This calculation assumes that 100% of man's exposure is assigned to the ambient water pathway. The only environmental monitoring data available on the DCB's inadequate as they are, suggest that man's exposure by inhalation of the material in air may be 3,000 to 15,000 times his exposure from water. Although it is desirable to arrive at a criterion level for water based on total exposure analysis, the data base for exposure pathways other than water is not sufficient to support a factoring of the ADI level calculated from ambient water assumptions.

The calculated level of 0.23 mg/l for any DCB isomer should be considered a total, i.e., total contamination by DCB isomers whether occurring singly or in combination should not exceed the criterion level. Pending the availability of better data on relative exposure by various routes and on carcinogenic risk, this level should be adequate to prevent adverse health effects from long-term ambient water exposures.

In summary, based on the use of chronic toxicologic test data in animals, and an uncertainty factor of 1000, the criterion level of DCB's (total) corresponding to the calculated total acceptable daily intake of 18.8 mg/kg, is 0.23 mg/l. Drinking water contributes 35% of the assumed exposure while eating contaminated fish products accounts for 65%. The criterion level for DCB can alternatively be expressed as 0.35 mg/l if exposure is assumed to be from the consumption of fish and shellfish products alone.

DICHLOROETHYLENES

Criteria Summary:

Freshwater Aquatic Life

For 1,1-dichloroethylene, the criterion to protect freshwater aquatic life, (as derived using procedures other than the Guidelines), is 530μg/1 as a 24-hour average and the concentration should not exceed 1,200μg/1 at any time.

For 1,2-dichloroethylene, the criterion to protect freshwater aquatic life, (as derived using procedures other than the Guidelines), is 620μg/1 as a 24-hour average and the concentration should not exceed 1,400μg/1 at any time.

Saltwater Aquatic Life

For 1,1-dichloroethylene, the criterion to protect saltwater aquatic life, (as derived using procedures other than the Guidelines), is 1,700μg/1 as a 24-hour average and the concentration should not exceed 3,900μg/1 at any time.

For saltwater aquatic life, no criterion for 1,2-dichloroethylene, can be derived using the guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to 1,1-dichloroethylene through ingestion of

water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of 1,1-dichloroethylene estimated to result in additional lifetime cancer risks ranging from no additional risk to 1 in 100,000 are presented in the Criterion Formulation section of this document. The agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10−7 with corresponding criteria of 1.3 μg/l, 0.13μg/l, and 0.013μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for either 1,1-dichloroethylene or 1,2-dichloroethylene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, results obtained for structurally similar compounds provide a way to estimate a criterion. For tetrachloroethylene and saltwater organisms and for trichloroethylene and freshwater organisms the Final Chronic Value is greater than 0.44 times the Final Acute Value, even though chronic values are available for the mysid shrimp and *Daphnia magna*, respectively. Therefore, this relationship is assumed in order to estimate criteria for both dichloroethylenes and freshwater organisms and 0.44 times the Final Acute Value is used.

Both a Final Fish Acute Value and a Final Invertebrate Acute Value are available for 1,1-dichloroethylene, and the Final Acute Value is based on the lower invertebrate value. Although a Final Fish Acute Value is available for 1,2-dichloroethylene, no invertebrate data are available. In all cases for di-, tri- and tetrachloroethylenes in which both Final Fish and Final Invertebrate Acute Values are available, the invertebrate species value is lower. Therefore the missing acute data for invertebrates and 1,2-dichloroethylene is important. In deriving an estimated criterion, the relative sensitivity of fish and invertebrate species for 1,1-dichloroethylene is assumed to hold for 1,2-dichloroethylene as well. For 1,1-dichloroethylene the Final Invertebrate Acute Value divided by the Final Fish Acute Value is 1,200/16,000=0.075. Multiplying this value times the Final Fish Acute Value for 1,2-dichloroethylene results in an estimated Final Invertebrate Acute Value of 0.075×19,000μg/l=1,400μg/l. Thus the Final Acute Value for 1,2-dichloroethylene is 1,400μg/l. Multiplying the Final Acute Value of 1,400μg/l by 0.44 gives 620μg/l.

The maximum concentration of 1,1-dichloroethylene is the Final Acute Value of 1,200μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,1-dichloroethylene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 530μg/l as a 24-hour average and the concentration should not exceed 1,200μg/l at any time.

The maximum concentration of 1,2-dichloroethylene is the estimated Final Acute Value of 1,400μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,2-dichloroethylene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 620μg/l as a 24-hour average and the concentration should not exceed 1,400μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1,1-dichloroethylene

Final Fish Acute Value=16,000μg/l
Final Invertebrate Acute Value=1,200μg/l
Final Acute Value=1,200μg/l
Final Fish Chronic Value=greater than 210μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=greater than 800,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=greater than 210μg/l
0.44×Final Acute Value=530μg/l

1,2-dichloroethylene

Final Fish Acute Value=19,000μg/l
Final Invertebrate Acute Value=not available
Final Acute Value=19,000μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=not available
0.44×Final Acute Value=8,400μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for either 1,1- or 1,2-dichloroethylene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, results obtained for structurally similar compounds indicate how a criterion may be estimated. For tetrachloroethylene and saltwater organisms and for trichloroethylene and freshwater organisms the Final Chronic Value is greater than 0.44 times the Final Acute Value, even though chronic values are available for the mysid shrimp and *Daphnia magna*, respectively. Therefore, this relationship is assumed in order to estimate a criterion for dichloroethylenes and saltwater organisms and 0.44 times the Final Acute Value is used.

Both a Final Fish Acute Value and a Final Invertebrate Acute Value are available for 1,1-dichloroethylene, and the Final Acute Value is equal to the lower invertebrate value. Because neither a Final Fish Acute Value nor a Final Invertebrate Acute Value is available for 1,2-dichloroethylene, no criterion can be derived.

The maximum concentration of 1,1-dichloroethylene is the Final Acute Value of 3,900μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 1,1-dichloroethylene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 1,700μg/l as a 24-hour average and the concentration should not exceed 3,900μg/l at any time.

No saltwater criterion can be derived for 1,2-dichloroethylene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

1,1-dichloroethylene

Final Fish Acute Value=37,000μg/l
Final Invertebrate Acute Value=3,900μg/l
Final Acute Value=3,900μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=greater than 710,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=greater than 710,000μg/l
0.44×Final Acute Value=1,700μg/l

1,2-dichloroethylene

Final Fish Acute Value=not available

Final Invertebrate Acute Value=not available

Final Acute Value=not available

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=not available

Final Plant Value=not available

Residue Limited Toxicant Concentration=not available

Final Chronic Value=not available

0.44×Final Acute Value=not available

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." 1,1-Dichloroethylene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of 1,1-dichloroethylene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of 1,1-dichloroethylene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria for 1,1-dichloroethylene at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/gl)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.013	0.13	1.3
Consumption of fish and shellfish only	0	0.214	2.14	21.4

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1000, and so forth.

[2] Approximately 7 percent of the 1,1-dichloroethylene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 8-fold. The remaining 93 percent of 1,1-dichloroethylene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of 1,1-dichloroethylene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding 1,1-dichloroethylene concentrations and, (2) occurring solely from assumption of aquatic life grown in the waters containing the corresponding 1,1-dichloroethylene concentrations. Because data indicating other sources of 1,1-dichloroethylene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Summary of Pertinent Data

Maltoni [1] exposed mice to 25 ppm via inhalation for 4 hrs/day, 4.5 days/week for 1 year. The interim report summarized the results after 82 weeks or 1.64 years. The control males had a kidney adenocarcinoma incidence of 0/126 and the treated males had an incidence of 16/98. The fish bioaccumulation factor is 6.9.

The parameters of the extrapolation model are:

nt=16
NT=98
nc=0
NC=126
Le=82 weeks
le=52 weeks
d=25×4/24×4.5/7×.04=1.0714 ppm
w=0.025 kg (not needed)
L=90 weeks
R=6.9
D=1.0714×52/82=0.67944 ppm
t=82/90=0.91111
t^3=0.75633
Dt^3=0.51388 ppm
B=1/.51388 in [(1-0/126)/(1-16/98)]=0.34686 (in terms of risk per ppm)

For air exposures in units of ppm, no species conversion factor is necessary. Therefore for humans the concentration, X, giving a risk, R, of 10^{-5} is X = R/B = 10^{-5}/.34686 = 2.8830×10^{-5} ppm.

Since the air concentration corresponding to 1 ppm of DCE is 4×10^3μg/m³ and since people breathe an average of 24 m³/day of air, the daily intake of DCE that would result in a lifetime risk of 10^{-5} is:

2.8830×10^{-5} ppm×4×10^3μg/m³ per ppm×24m³/day=2.7677μg.day

If it is assumed that the fraction of the DCE intake reaching the target site is the same whether it is administered via limitation or ingestion of water and fish, a daily DCE intake of 2.768μg through water and fish alone would also cause a cancer risk of 10^{-5}. The water concentration giving this intake is:

$$C = \frac{2.7677 \text{ ug/day}}{(2 + 6.9 \times .0187) \text{ liters/day}}$$

= 1.2999 μg/l

≃ 1.3 μg/l

[1] Maltoni, C. 1977. Recent findings on the carcinogenicity of chlorinated olefins. Environ. Health Perspect 21:1.

2,4-DICHLOROPHENOL

Criteria Summary:

Freshwater Aquatic Life

For 2,4-dichlorophenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.4μg/l as a 24-hour average and the concentration should not exceed 110μg/l at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for 2,4-dichlorophenol can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the prevention of adverse effects due to the organoleptic properties of 2,4-dichlorophenol in water, the criteria is 0.5μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of 2,4-dichlorophenol is the Final Acute Value of 110μg/l and the 24-hour average concentration is the Final Chronic Value of 0.4μg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 2,4-dichlorophenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.4μg/l as a 24-hour average and the concentration should not exceed 110μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=770μg/l

Final Invertebrate Acute Value=110μg/l

Final Acute Value=110μg/l

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=not available

Final Plant Value=50,000μg/l

Residue Limited Toxicant Concentration=not available

Final Chronic Value=0.4μg/l for tainting

0.44×Final Acute Value=48μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for 2,4-dichlorophenol using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

None available.

Human Health

Insufficient data exists to indicate that 2,4-DCP is a carcinogenic agent. One study was designed to detect promoting activity, and the effect of 2,4-DCP as a primary carcinogen could not be evaluated. In fact, only minimal health effects data exist on the acute and chronic effects of 2,4-DCP. Only one chronic study was found in which a chronic (6-month) no-effect level for 2,4-DCP of 1,000μg/l of diet for mice, which is equivalent to 100mg/kg body weight per day was determined. For water, a concentration of approximately one-half the dietary intake will result in equivalent dosage on a body weight basis, assuming a fluid intake two times the dry matter intake.

If food sources are not included, the maximum no-effect level of 2,4-DCP in water for mice would be 500μg/l. Applying an uncertainty factor of 10^{-3} × maximum no-effect level as suggested by the National Academy of Sciences Safe Drinking Water Committee would result in a criterion for human health of 500μg/liter, which is approximately 250 times greater than the threshold odor concentration.

However, in addition to exposure through drinking water, additional exposure to 2,4-DCP through the daily ingestion of 18.7 g of fish and shellfish products exists. Therefore, based on the assumption of an intake of 2 l of drinking water per day at a level of 500μg/l, and a fish bioconcentrating value of 37, the total amount of 2,4-DCP exposure through both routes is 371μg/day:

$$\frac{2 \times 500\ \mu g/day}{2 + (37 \times 0.0187)} = 371\ \mu g/day$$

Human health is a subject measurement in many respects. The organoleptic effect of 2,4-DCP could conceivably alter human health by causing a decrease in water consumption. This might be of particular importance to individuals with certain renal diseases or in instances where dehydration occurs as a result of vigorous exercise, manual labor, or hot weather. Although two investigators reported that low concentrations of 2,4-DCP caused discernible odor, neither indicated if the threshold odor concentration made water unacceptable for consumption. In view of the wide disparity between odor threshold concentrations and available toxicity information, the criterion recommended is based on organoleptic effects. It is suggested that a 2,4-DCP water concentration of 0.5μg/l would be low enough to prevent objectionable organoleptic effects for most people and still be far below minimal no-effect concentrations determined in laboratory animals.

In conclusion, two criteria can be proposed. Based on the prevention of adverse organoleptic effects, the interim criterion recommended for 2,4-dichlorophenol is 0.5μg/l in water. Based on human health effects alone, the interim criterion recommended is 371μg/l.

2,4-DIMETHYLPHENOL

Criteria Summary:

Freshwater Aquatic Life

For 2,4-dimethylphenol, the criterion to protect freshwater aquatic life, as derived using the Guidelines, is 38μg/l as a 24-hour average and the concentration should never exceed 86μg/l at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for 2,4-dimethylphenol can be derived using the Guidelines and there are insufficient data to estimate a criterion using other procedures.

Human Health

Due to a lack of sufficient definitive data on mammalian toxicology and human health effects, a criterion to protect human health from toxic effects due to exposure to 2,4-dimethylphenol ingested through water and through contaminated aquatic organisms cannot be set at this time. In order to protect public health, exposure to this compound should be minimized as soon as possible.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of 2,4-dimethylphenol is the Final Acute Value of 86μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For 2,4-dimethylphenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 38μg/l as a 24-hour average and the concentration should not exceed 86μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=2,200μg/l

Final Invertebrate Acute Value=86μg/l

Final Acute Value=86μg/l

Final Fish Chronic Value=160μg/l

Final Invertebrate Chronic Value=not available

Final Plant Value=290,000μg/l

Residue Limited Toxicant Concentration=not available

Final Chronic Value=160μg/l

0.44×Final Acute Value=38μg/l

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for 2,4-dimethylphenol can be derived using the Guidelines and there are insufficient data to estimate a criterion using other procedures.

Human Health

In quantitative assessment of carcinogenicity, there are a number of special conditions which render the extrapolation of animal carcinogenesis data to man inappropriate (see Methodology Document). In the present case, the condition which applies is that the route of administration is inappropriate in terms of conceivable human exposure.

Only one study was found which indicated that 2,4-dimethylphenol could be carcinogenic in mammals; Sutter mice, a strain highly susceptible to skin carcinomas, were used.

In these experiments, 5 mg or 2.5 mg of 2,4-dimethylphenol in benzene, applied twice a week to the backs of shaved mice, produced papillomas and carcinomas of the skin at the site of application. Even though the compound is known to be rapidly absorbed, systemic effects or internal tumors were not reported. Additionally, the possible contribution of other chemicals to the response observed cannot be discounted. A solvent control (benzene) was not run, and the mice were housed in wood cages treat-

ed with creosote, which may have initiated the carcinogenic response.

In addition, the Carcinogen Assessment Group, U.S. EPA, Washington, D.C. concluded that the above data

regarding possible carcinogenic effects (via initiation) of 2,4-dimethylphenol are inconclusive. The report did indicate that 2,4-dimethylphenol was a promoting agent. Although promoters have a potential carcinogenic risk to humans, there is no dose-response data with which to formulate a quantitative risk extrapolation.

Is is inappropriate to extrapolate from results obtained from the use of high concentrations in skin painting studies to an estimate of the possible carcinogenic effects of the ingestion of small amounts of 2,4-dimethylphenol in water. The only data found for the ingestion of 2,4-dimethylphenol were an LD50 for mice of 809 mg per kg, and an LD50 for rats of 3,200 mg per kg.

The National Academy of Sciences concluded the following concerning drinking water and health:

2,4-Dimethylphenol appears to be a topical cocarcinogen, but its role as a primary cancer-producing agent is uncertain. Its potential role in cancer production warrants consideration of further testing. An *in vitro* mutagenicity assay should be carried out to further evaluate its mutagenic potential.

In view of the relative paucity of data on the mutagenicity, carcinogenicity, teratogenicity and long-term oral toxicity of 2,4-dimethylphenol, estimates of the effects of chronic oral exposure at low levels cannot be made with any confidence. It is recommended that studies to produce such information be conducted before limits in drinking water are established.

We recommend that a criterion should not be set for 2,4-dimethylphenol in water until definitive data are obtained. In order to protect public health, exposure of humans to this compound should be minimized.

FLUORANTHENE

Criteria Summary:

Freshwater Aquatic Life

For fluoranthene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 250μg/l as a 24-hour average and the concentration should not exceed 560μg/l at any time.

Saltwater Aquatic Life

For fluoranthene the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.30μg/l as a 24-hour average and the concentration should not exceed 0.69μg/l at any time.

Human Health

For the protection of human health from the toxic properties of fluoran=threne exposure through water, the ambient water quality criterion is determined to be 200μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for fluoranthene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

Data for fluoranthene and saltwater organisms can be used to estimate a criterion.

For fluoranthene and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from results of a life cycle test with the mysid shrimp. Therefore, a reasonable estimate of a criterion for fluoranthene and freshwater organisms would be 0.44 times the Final Acute Value.

The maximum concentration for fluoranthene is the Final Acute Value of 560μg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For fluoranthene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 250μg/l as a 24-hour average and the concentration should not exceed 560μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=560μg/l

Final Invertebrate Acute Value=13,000μg/l

Final Acute Value=560μg/l

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=not available

Final Plant Value=54,000μg/l

Residue Limited Toxicant Con=centration=not available

Final Chronic Value=54,000μg/l

0.44×Final Acute Value=250μg/l

Saltwater Aquatic Life

The maximum concentration of fluoranthene is the Final Acute Value of 0.69μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For fluoranthene the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 30μg/l as a 24-hour average and the concentration should not exceed 0.69μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=not available

Final Invertebrate Acute Value=0.69μg/l

Final Acute Value=0.69μg/l

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=3.1μg/l

Final Plant Value=45,000μg/l

Residue Limited Toxicant Concentration=not available

Final Chronic Value=3.1μg/l

0.44 x Final Value=0.30μg/l

Human Health

Calculation of the criterion takes into consideration the contribution of dietary and airborne sources of fluoranthene. Once these factors are accounted for, this procedure leads to the conclusion that 200μg/l of fluoranthene in drinking water would represent an acceptable level of exposure. It must be emphasized, however, that the criterion is based on chronic toxicity data with mortality being the endpoint, and applies only to situations where exposure occurred to fluoranthene alone. In environmental situations, it is well established that fluoranthene is found in the presence of numerous PAH's; a situation having important implications for potential toxic interactions.

Several studies have clearly shown that fluoranthene possesses no carcinogenic activity, and is neither a tumor initiator nor a tumor promoter (see Carcinogenicity section). However, two carefully conducted studies have shown that fluoranthene when applied to mouse skin together with much smaller quantities of benzo(a)pyrene could act as a cocarcinogen to increase tumorgenic response. These data do not permit a quantitative estimation of health risks incurred by this type of biological phenomenon. Nevertheless, because fluoranthene is present in environmental mixtures together with other PAH's (including several carcinogens) it may pose an additional risk to the population exposed. In view of the cocarcinogenic and anticarcinogenic properties of several environmental PAH's, the degree of added risk, if one exists, cannot be easily determined on the basis of our present scientific knowledge.

Inadequacies in the current scientific data base prevent the formulation of a drinking water criterion for fluoranthene based on potential cocarcinogenicity. However, it would seem prudent to temporarily limit the level of fluoranthene in drinking water to no more than the acceptable concentration of the sum of all non-fluoran-

thene PAH's. In addition, since environmental exposures to fluoranthene will almost certainly involve concomitant exposure to carcinogenic PAH's, their potential interaction should be considered in future research and health criteria development.

HEPTACHLOR

Criteria Summary:

Freshwater Aquatic Life

For heptachlor the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0015μg/l as a 24-hour average and the concentration should not exceed 0.45μg/l at any time.

Saltwater Aquatic Life

For heptachlor the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0036μg/l as a 24-hour average and the concentration should not exceed 0.05μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to heptachlor through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of heptachlor estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 0.23 ng/l, 0.023 ng/l, and 0.0023 ng/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of heptachlor is the Final Value of 0.45μg/l, which is based on the more acutely sensitive invertebrate organisms. Since 0.44 times the Final Acute Value (0.44×0.45μg/l=0.20μg/l) is not lower than the Final Chronic Value (0.0015μg/l), the latter is the recommended 24-hour average concentration.

For heptachlor the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0015μg/l as a 24-hour average and the concentration should not exceed 0.45μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=7.5μg/l
Final Invertebrate Acute Value=0.45μg/l
Final Acute Value=0.45μg/l
Final Fish Chronic Value=0.19μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=not available
Residue Limited Toxicant Concentration=0.0015μg/l
Final Chronic Value=0.0015μg/l
0.44×Final Acute Value=0.20μg/l

Saltwater Aquatic Life

To derive the criterion, the maximum concentration is the Final Acute Value of 0.05μg/l and the 24-hour average concentration is the Final Chronic Value of 0.0036μg/l. No important adverse effects on marine aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration. But some data for the pink shrimp indicate concern for this and related species.

For heptachlor the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0036μg/l as a 24-hour average and the concentration should not exceed 0.05μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=0.85μg/l
Final Invertebrate Value=0.05μg/l
Final Acute Value=0.05μg/l
Final Fish Chronic Value=0.12μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=1,000μg/l
Residue Limited Toxicant Concentration=0.0036μg/l
Final Chronic Value=0.0036μg/l
0.44×Final Acute Value=0.22μg/l

Human Health

Basis for the Criterion:

The proposed criterion for heptachlor/heptachlor epoxide in drinking water was derived from the extrapolation of the data presented by Davis (1965) [1] using a linear, non-threshold model. The extrapolation methodology can be found in the Methodology Document.

From this extrapolation the calculated dose of heptachlor/heptachlor epoxide in drinking water was found to be 0.23 nanogram per liter.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Heptachlor is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of heptachlor in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of heptachlor corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

[1] Davis, K. J. 1965. Pathology report on mice fed aldrin, dieldrin, heptachlor, or heptachlor epoxide for two years. Internal Memorandum to Dr. A. J. Lehman. U.S. Food Drug Admin.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7} (μg/l)	10^{-6} (μg/l)	10^{-5} (μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.0023	0.023	0.23
Consumption of fish and shellfish only	0	0.0023	0.023	0.23

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology document to the animal bioassay data presented in Appendix I. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] 98 percent of the heptachlor exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 5,200-fold. The remaining 2 percent of heptachlor exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of heptachlor, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding heptachlor concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding heptachlor concentrations.

Although total exposure information for heptachlor is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into amibient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

Summary of Pertinent Data

The FDA lifetime carcinogenicity study (Davis, 1965) of heptachlor epoxide at 10 ppm in the diet of C3Heb/Fe/J strain mice resulted in liver carcinomas in females in 77 of 81 treated animals and 2 of 54 controls. Using a fish bioaccumulation factor of 5,200, the water concentration estimated to result in a lifetime risk of 10^{-5} is calculated from the extrapolation model using the following parameters:

nt=77
NT=81
nc=2
NC=54
Le=104 weeks
le=104 weeks
d=$10\times10^{-6}\times0.13\times10^{-6}$ mg food per day/kg body weight=1.3 mg/kg/day
w=0.030 kg
L=104 weeks
R=5,200

The result is that the water concentration corresponding to a lifetime risk of 10^{-5} is 0.23 (0.233) nanograms/liter.

HEXACHLOROBUTADIENE

Criteria Summary:

Freshwater Aquatic Life

For freshwater aquatic life, no criterion for hexachlorobutadiene can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for hexachlorobutadiene can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to hexachlorobutadiene through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentration of hexachlorobutadiene estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 0.77μg/1, 0.077μg/1, and 0.0077μg/1, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for hexachlorobutadiene using the Guidelines because no Final Chronic Value for either fish of invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=16μg/l
Final Invertebrate Acute Value=8.7μg/l
Final Acute Value=8.7μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=not available
0.44 x Final Acute Value=3.8μg/l

No freshwater criterion can be derived for hexachlorobutadiene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Saltwater Aquatic Life

No saltwater criterion can be derived for hexachlorobutadiene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Human Health

Hexachlorobutadiene (HCBD) exhibits acute, subacute and chronic toxicity in animal test systems.

The kidney appears to be the organ most sensitive to HCBD. Chronic effects are observed at doses as low as 2 to 3 mg/kg/day in rats.

Renal tubular neoplasms were observed during a 2-year study in which 20 mg/kg/day was administered to rats in their diet. Single oral doses as low as 8.4 mg/kg have been observed to have a deleterious effect on the kidney.

The carcinogenic effects of renal tubular adenomas and adenocarcinomas were strongly demonstrated at the 20 mg/kg/day dosage. In addition, a dose-dependent increase in reversion rate was observed upon adding HCBD without activation to cultures of *S. typhimurium*. Although the observed rate was not quite double the background rate a mutagenic potential for HCBD is indicated.

The evidence of carcinogencity is sufficient to conclude that HCBD is a suspect human carcinogen. As carcinogens are generally assumed to have a non-threshold dose/response characteristic, the carcinogenic effect is the most significant exposure effect from which to estimate an ambient water quality criterion value.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Hexachlorobutadiene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of hexachlorobutadiene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of hexachlorobutadiene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table.

Concentration levels were derived assuming a lifetime exposure to various amounts of hexachlorobutadiene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding hexachlorobutadiene concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding hexachlorobutadiene concentrations. Because data indicating other sources of hexachlorobutadiene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the in-

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.077	0.077	0.77
Consumption of fish and shellfish only	0	0.0087	0.087	0.87

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to animal bioassay data presented in Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately 89 percent of the hexachlorobutadiene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 870-fold. The remaining 11 percent of hexachlorobutadiene exposure results from drinking water.

cremental risks associated with the indicated routes only.

Summary of Pertinent Data

In a 2-year feeding study in rats, Kociba (1977)[1] observed renal tubular adenomas and carcinomas in males with significantly higher incidence in animals fed 20 mg/kg/day (7/39) than control animals (1/90). Using a fish bioaccumulation factor of 870, the parameters of the extrapolation model are:

$n_1=7$
$N_1=39$
$n_2=1$
$N_2=9$
Le=730 days
le=669 days
d=20 mg/kg/day
w=0.610 kg
L=730 days
R=870

The result is that the water concentration should be less than 0.77 micrograms per liter in order to keep the individual lifetime risk below 10^{-5}.

HEXACHLOROCYCLOPENTADIENE

Criteria Summary:

Freshwater Aquatic Life

For hexachlorocyclopentadiene, the criterion to protect freshwater aquatic life, as derived using the Guidelines is 0.39μg/l as a 24-hour average and the concentration should not exceed 7.0μg/l at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the prevention of adverse effects due to the organoleptic properties of hexachlorocyclopentadiene in water, the criterion is 1.0μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of hexachlorocyclopentadiene is the Final Acute Value of 7.0μg/l and the 24-hour average concentration is the Final Chronic Value of 0.39μg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For hexachlorocyclopentadiene the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.39μg/l as a 24-hour average and the concentration should not exceed 7.0μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=7.0μg/l
Final Invertebrate Acute Value=not available
Final Acute Value=7.0μg/l
Final Fish Chronic Value=0.39μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=0.39μg/l
0.44×Final Acute Value=3.1μg/l

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for hexachlorocyclopentadiene can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

No data on the effects of hexachlorocyclopentadiene on saltwater organisms are available.

Human Health

As indicated earlier, there are no epidemiologic studies nor suitable chronic toxicity studies in mammals from which threshold levels for chronic effects could be derived. Very little is known regarding potential hex exposures through ingestion of contaminated food or water. In the envrionment hex has been detected only in specific bodies of water near points of industrial discharges. There is no data on hex levels in drinking or untreated water.

Based on the available and cited literature, there is insufficient evidence to categorize this compound as a carcinogen or non-carcinogen. There has not been a satisfactory study of the effects of chronic oral exposure to hex.

One test consisted of only one species (rats) with a duration of exposure of only six months. No neoplasms were reported, however the duration of the study would not have been sufficient for a proper evaluation of carcinogenicity.

Hex has been tested for mutagenicity and reported non-mutagenic in both short-term *in vitro* mutagenic assays and in a mouse dominant lethal study. No epidemiologic studies or case reports examining the relationship between exposure to hex and cancer incidences could be found in the literature. Therefore, there is virtually no information regarding the carcinogenic potential of chronic exposure to hex. In selecting hex for future chronic toxicity testing, National Cancer Institute recognized these data voids.

Although one study reported the effects of chronic low-dose inhalation of hex, its applicability in deriving water quality guidelines is unclear. Furthermore, with the exception of very limited data on hex in water near points of discharge, there appears to be no information on hex levels in water bodies. What is needed is a method for converting the results of respiratory exposure experiments into equivalent dosages from water.

There is a model by which the threshold limit values (TLV' s) for industrial substances in air may be used in establishing drinking water standards. The model assumes that, for any given inhaled dose, an equivalent ingested dose from ingested water can be derived using reasonable estimates of daily air and water intakes and corresponding respiratory and gastrointestinal absorption rates. In the absence of suitable chronic ingestion studies of hex, this model will be used to estimate suitable limits for hex in water based on the established threshold

[1] Kociba, R. J., 1977. Results of a two-year chronic toxicity study with hexachlorobutadiene in rats. Am. Ind. Hyg. Assoc. *38*:589.

limit value expressed as milligrams per cubic meter of air.

The threshold limit of 0.11 mg/m³ (0.01 ppm) hex represents what is believed to be a maximal concentration to which a worker may be exposed for 8 hours per day, 5 days per week over his working lifetime without hazard to health or well-being. To the TLV, are applied terms expressing respiratory volume during an 8-hour period (assumed to be 10 m³) and a respiratory absorption coefficient appropriate to the substance under consideration. As in the case of hex where absorption rates are unknown, 100 percent absorption is assumed. In addition, the 5 day per week occupational exposure is often converted to a 7 day per week equivalent in keeping with the more continous pattern of exposure to drinking water.

According to the model, the amount of hex that may be taken into the bloodstream and presumed to be noninjurious and which, hence, may be taken in water each day is:

0.11 mg/m³	x 10 m³	x 1.0	x 5/7 week	= 0.7857 mg/d
(TLV)	Respiratory Intake Term	Respiratory Absorption Coefficient	Proportion of week Exposed	Maximum Noninjurious Intake

To calculate the quivalent amount of hex in ambient water, the model assumes a maximal daily intake of 2 liters of water per day, the consumption of 18.7 grams of fish/shellfish per day, a bioconcentration factor of 3.2 for fish and 100 percent absorption.

(X)	x (2 + 3.2(0.0187)) x	1.0	=	0.7857
Upper Intake Limit --	Oral Intake Term	Gastrointestinal Absorption Coefficient		Maximum Noninjurious Intake

Solving for X, the value derived is 0.38 mg/l or 380μg/l. According to Stokinger and Woodward, who developed the model, "This derived value represents an approximate limiting concentration for a healthy adult population; it is only a first approximation in the development of a tentative drinking water criterion * * * several adjustments in this value may be necessary * * * Other factors, such as taste, odor and color may outweigh health considerations because acceptable limits for these may be below the estimated health limit."

It should also be noted that the basis for the above recommended limit, the TLV for hex, is set on the basis of avoidance of irritation, rather than chronic effects. Should chronic effects data become available, both TLV's and recommendations based on them will warrant reconsideration.

A single study of chronic oral toxicity in white rats reported no adverse effects (specifically changes in peripheral blood cells, ascorbic acid content of the adrenals, conditioned reflexes of the animals, or histological structure of the organs) following daily oral administration of doses up to 4μg/l of hex in aqueous solution. Animals receiving the highest dosage, 40μg/l, showed neutropenia and lympho-cytosis which the investigators thought possibly attributable to mobilization of the protective forces of the organism in response to this dose. Such findings imply adverse effects at levels as low as 10 percent of the tentative drinking water standard based on the Stokinger and Woodward model. Hex in concentrations of 1.4 to 1.6μg/l is capable of altering the smell and taste of water. Based on these organoleptic effects, these investigators proposed a maximum permissible concentration of 1μg/l. Stokinger and Woodward themselves noted that oftentimes "other factors, including taste, odor and color may outweigh health considerations because acceptable limits for these may be well below the estimated health limit".

Because chronic effects in a mammalian species (rats) have been documented at water concentrations of hex as low as 40μg/l, it is obvious that an acceptable water quality criterion should be well below this level. Thus, a reasonable safety factor of 10 to 100 applied to 40μg/l would place an appropriate criterion recommendation in the range of 4.0–0.4μg/l in water.

No adverse effects on humans or mammals have been reported to be caused by hex concentrations lower than approximately 1.0μg/l. Therefore, based on avoidance of alteration in smell and aftertaste in water, a criterion of 1.0μg/l of hex in water is tentatively suggested. This level should be adequate for protection of public health. It is to be stressed that this criterion is based on inadequate chronic effects data and should be re-evaluated upon completion of chronic oral toxicity studies.

LEAD

Criteria Summary:

Freshwater Aquatic Life

For lead, the criterion to protect freshwater aquatic life as derived using the Guidelines is "$e^{(1.51 \cdot \ln(\text{hardness})-3.37)}$" as a 24-hour average (see the figure "24-hour average lead concentration vs. hardness") and the concentration should not exceed "$e^{(1.51 \cdot \ln(\text{hardness})-1.39)}$" (See the figure "maximum lead concentration vs. hardness") at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for lead can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

for the protection of human health from the toxic properties of lead ingested through water and through contaminated aquatic organisms, the ambient water criterion for lead is 50 μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of lead is the Final Acute Value of $e^{(1.51 \cdot \ln(\text{hardness})-1.39)}$ and the 24-hour average concentration is the Final Chronic Value of $e^{(1.51 \cdot \ln(\text{hardness})-1.37)}$. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

Summary of Available Data

Final Fish Acute Value=$e^{(1.51 \cdot \ln(\text{hardness})+2.50)}$

Final Invertebrate Acute Value=$e^{(1.51 \cdot \ln(\text{hardness})-1.39)}$

Final Acute Value=$e^{(1.51 \cdot \ln(\text{hardness})-1.39)}$

Final Fish Chronic Value=$e^{(1.51 \cdot \ln(\text{hardness})-3.37)}$

Final Invertebrate Chronic Value=$e^{(1.51 \cdot \ln(\text{hardness})-1.75)}$

Final Chronic Value=$e^{(1.51 \cdot \ln(\text{hardness})-1.37)}$

Final Plant Value= 500μg/l

Residue Limited Toxicant Concentration=not available

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for lead can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of lead.

Final Fish Acute Value=not available

Final Invertebrate Acute Value=50μg/l

Final Acute Value=50μg/l

Human Health

The approach that will be taken here in assessing the impact of lead in water on human health is basically the same as has been taken by the U.S. EPA for lead in air. The critical target organ or system must first be identified. Then, the highest internal dose of lead that can be tolerated without injury to the target organ must be specified. Finally, the impact of lead in water on the maximum tolerated internal dose must be estimated, as well as the likely consequences of specific reductions in the maximum allowable concentration of lead in water.

In identifying the critical organ or system, great reliance is placed on the concentration of lead in the blood (PbB) as an index of internal dose. Such an indirect measurement is necessary because of the multi-media character of lead intake. It is virtually impossible to measure total lead input in people in any meaningful way. To do so would require long-term balance studies because past experience has shown that intake and output fluctuate greatly from day to day. Furthermore, it would be necessary to conduct such studies on large numbers of free-living subjects, given the influences of chemical and physical variables in the numerous environmental forms of lead. Variables have a substantial influence on the rate and degree of lead uptake from the external environment. Some groups have proposed alternatives to PbB as a measure of internal dose, e.g., FEP and tooth lead. FEP is not suitable because it is a biological response to lead. As such, it is subject to influences other than lead, notably iron deficiency. Tooth lead is a potentially useful index of lead exposure, but with the present state of art being what it is, tooth lead is difficult to interpret. It only provides an integrated profile of past lead exposure. One is not able to say when the exposure occurred. It has the additional limitation of not being available on demand. Teeth are shed spontaneously only in childhood. Beyond all that is the fact that we have only a very small data base for dose-effect and dose-response using any measure of dose other than PbB. The use of PbB as a measure of internal dose is widely accepted, simply because nothing better is available.

Having specified that PbB is the best measure of internal dose currently available, the next question concerns the least PbB at which adverse health effects occur. Two recent documents have been published in which judgments were rendered in this regard (Table 12). It will be noted that the estimates are strikingly similar. The estimated no-effects levels are based on limited populations and probably are lower to some indefinable degree in the total population at risk. The expert panels that made these estimates were largely composed of different individuals, although there was some overlap. Slightly more information was available to the U.S. EPA panel than to the World Health Organ. panel since it reviewed literature only through mid-1977 whereas the World Health Organ. expert groups reviewed literature through much of 1976. In addition, the U.S. EPA performed statistical calculations based on the known distribution of blood lead levels in the United States.

Both sets of data in Table 12 are in error in one regard. They use the term "anemia" inappropriately under the "Effect" column. What they really mean is "decrement in hemoglobin." Anemia is a clinical term used to denote a degree of hemoglobin decrement which is below the normal range for that class of individuals, e.g., men or children.

The question that arises in considering Table 12 is which is the critical effect? Precisely the same issue confronted the U.S. EPA in its deliberations concerning establishment of a national ambient air quality standard for lead. It focused on the lead effects in children since they are more sensitive than adults.

TABLE 12.—*Summary of Lowest PbB's Associated With Observed Biological Effects in Various Population Groups*

Lowest observed effect level (μg Pb/100 ml blood)	Effect	Population group
10	ALAD inhibition	Children and adults.
15–20	Erythrocyte protoporphyrin elevation	Women and children.
25–30	Erythrocyte protoporphyrin elevation	Adult males.
40	Increased urinary ALA excretion	Children and adults.
40	Anemia	Children.
40	Coproporphyrin elevation	Adults and children.
50	Anemia	Adults.
50–60	Cognitive (CNS) deficits	Children.
50–60	Peripheral neuropathies	Adults and children.
80–100	Encephalopathic symptoms	Children.
100–120	Encephalopathic symptoms	Adults.

No-Detected Effect Levels in Terms of PbB

No detected effect level (μg Pb/100 ml blood)	Effect	Population group
10	Erythrocyte ALAD inhibition	Adults, children.
20–25	FEP	Children.
20–30	FEP	Adult, female.
25–35	FEP	Adult, male.
30–40	Erythrocyte ATPase inhibition	General.
40	ALA excretion in urine	Adults, children.
40	CP excretion in urine	Adults.
40	Anaemia	Children.
40–50	Peripheral neuropathy	Adults.
50	Anaemia	Adults.
50–60	Minimal brain dysfunction	Children.
60–70	Minimal brain dysfunction	Adults.
60–70	Encephalopathy	Children.
80	Encephalopathy	Adults.

Quite properly, it ruled that the maximum safe blood lead level for any given child should be somewhat lower than the threshold for a decline in hemoglobin level (40μg Pb/dl). In considering how much lower this limit should be, the U.S. EPA cited the opinion of the Center for Disease Control, as endorsed by the American Academy of Pediatrics, that the maximum safe blood lead level for any given child should be 30μg/dl. Based upon epidemiological and statistical considerations, the U.S. EPA estimated that if the geometric mean PbB were kept at 15μg/dl, 99.5 percent of children would have PbB's≤30μg/dl. This position seems prudent and reasonable. It provides a substantial margin of safety which accommodates minor excursions in lead exposure due to adventitious sources. Controls on lead in obligatory media (e.g., air and water) do not of course protect children from the hazards of pica for lead-base paint chips or soil and dust contaminated with lead from such sources as fallout from the smoke zone of lead smelters. These, however, are separate problems which must be dealt with appropriately by responsible agencies.

In its deliberations concerning an ambient air lead standard, the U.S. EPA estimated that the contribution of sources other than air to PbB is 10 to 12μg/dl. This is presumably composed overwhelmingly of dietary sources which, in turn, is composed of both food and water.

The next question concerns the contribution of water to lead exposure. It is unfortunate that only three useful studies of the interrelationship between PbB and lead in drinking water are available. There is an obvious need for more such work. Overall, the Moore, et al. study, the one by Hubermont, et al., and the calculations made from U.S. EPA data collected in the Boston area are credible because they are consistent with other information concerning the curvilinear relationship between PbB and air Pb. The implication of the equation describing the relationship between PbB and water lead is that with increasing lead in water the incremental rise in PbB becomes progressively smaller as with air lead vs. PbB and dietary lead vs. PbB to Lead from Diet Versus Air to PbB. The water lead vs. PbB relationship differs in one significant respect, however, from the air lead vs. PbB relationship in that the baseline PbB (0 water PbB) is independent of the contribution of water lead to PbB. Thus, regardless of whether one starts with a baseline PbB of 11μg/dl, as was indicated in the Moore, et al. study or whether one starts at some other PbB level, e.g., 20μg/dl, the add-on PbB from any given level in water will be the same. Such is not the case in the Azar analysis of air Pb vs. PbB (see Section on "Contributions of Lead from Diet vs. Air to PbB"). Here, the higher the baseline, the less the contribution of any specific air Pb. This is because log PbB (not PbB) is proportional to baseline PbB + log air concentration. Future research may provide better insight into whether this discrepancy is real and, if so, why. The question is of some practical importance. For instance, if you have a baseline PbB (no lead in water) of 30μg/dl such as in a child acquiring lead from paint, it would be of some importance to know whether an additional increment of lead in water would have the same impact on PbB as it would in a child having a baseline PbB of 10μg/dl. An Azar-type model would suggest a lesser impact starting from the higher baseline PbB.

So far as a specific recommendation regarding a revised water standard for lead is concerned, one is tempted to duck the whole issue by simply recommending more research. However, that might defer the recommendation indefinitely. A position must be taken using available data. Beginning with the assumption that a PbB of 12μg/dl is essentially attributable to food and water and that the average lead content of water consumed is 10μg/l, approximately 5μg Pb/dl blood is attributable to the water that is used in food and beverage preparation and in direct consumption. If the water Pb were consistently consumed at the present Pb standard of 50μg/l instead of at 10μg/l, an additional contribution of approximately 3.4μg/dl to PbB would result. This would yield a total PbB of 12+3.5 or 15.4μg/dl, the approximate maximum geometric mean PbB compatible with keeping 99.5 percent of the population of the population under PbB=30μg/dl. Thus, based on most recent data, the present water standard of 50μg Pb/l may be viewed as representing the upper limit of acceptability.

All the assumptions that have been made in arriving at an estimate of the impact of lead in water on PbB have been on the conservative side. For instance, unpublished data from the Commission of the European Communities suggest that the impact of lead in water on PbB is appreciably less than has been estimated from published data used in this document.

Furthermore, data from a study of the effect of lead in water on the PbB of a population of children in a relatively small town are reassuring. They indicate that among children whose water supply contained 50 to 180μg Pb/l, PbB's averaged 17.2μg/dl.

TABLE 13.—*Relation of PbB to Lead in Water Among Children in Bennington, Vt.*

Concentration of lead in water (μg/l)	No. of children	Mean blood lead level (μg/dl)
50–59	14	18.9
60–69	8	16.8
70–79	10	18.0
80–89	4	18.5
100–109	3	16.0
110–119	2	21.5
130–139	2	16.0
170–179	3	15.0
Total	46	17.2

Finally, there remains the issue of the carcinogenic effects of lead. Using data from one species of laboratory animal (the rat) it was possible to construct a seemingly valid dose-response curve and to calculate a level of lead intake which would predict an incidence of cancer in 1:100,000 people. This calculated level of lead intake, 29μg/kg of diet, poses some problems which must be confronted by the EPA Carcinogen Assessment Group. Since this estimate includes lead from all sources, its implications are beyond the scope of this document. It should be noted, however, that the International Agency for Research on Cancer, (IARC), Lyon, France considers the experimental animal evidence to be of dubious significance with regard to man.

The IARC summary statement, quoted in part earlier in this document, is as follows:

> There is no evidence to suggest that exposure to lead salts causes cancer of any site in man. However, only one epidemiological study of the relationships between exposure to lead and the occurrence of cancer has been reported. It must be noted that the level of human exposure equivalent to the levels of lead acetate producing renal tumors in rats is 810 mg per day (550 mg Pb). This level appears to exceed by far the maximum tolerated dose for man.

Criteria Summary:

Freshwater Aquatic Life

For freshwater aquatic life, no criterion for N-nitrosodiphenylamine can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for N-nitrosodiphenylamine can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to N-nitrosodimethylamine through ingestion of water and contaminated aquat-

ic organisms, the ambient water concentration is zero. Concentrations of N-nitrosodimethylamine estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 0.026μg/l, 0.0026μg/l, and 0.00026μg/l, respectively.

For the maximum protection of human health from the potential carcinogenic effects of exposure to N-nitrosodiethylamine through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of N-nitrosodiethylamine estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6} or 10^{-7} with corresponding criteria of 0.0092μg/l, 0.00092μg/l, and 0.000092μg/l, respectively.

For the maximum protection of human health from the potential carcinogenic effects of exposure to N-nitrosodi-n-butylamine through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of N-nitrosodi-n-butylamine estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6} or 10^{-7} with corresponding criteria of 0.013μg/l, 0.0013μg/l, and 0.00013μg/l, respectively.

For the maximum protection of human health from the potential carcinogenic effects of exposure to N-nitrosopyrrolidine through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of N-nitrosopyrrolidine estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6} or 10^{-7} with corresponding criteria of 0.11μg/l, 0.011μg/l, and 0.0011μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for N-nitrosodiphenylamine using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion. However, the results of the incomplete chronic test with *Daphnia magna* indicate that the Final Chronic Value would be lower than 9.4μg/l.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

N-nitrosodiphenylamine

Final Fish Acute Value=820μg/l
Final Invertebrate Acute Value=310μg/l
Final Acute Value=310μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=less than 9.4μg/l
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=less than 9.4μg/l
0.44 × Final Acute Value=140μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for N-nitrosodiphenylamine using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

N-nitrosodiphenylamine

Final Fish Acute Value=490,000μg/l
Final Invertebrate Acute Value=not available
Final Acute Value=490,000μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=not available
Residue Limited Toxicant Concentration=not available
Final Chronic Value=not available
0.44 × Final Acute Value=220,000μg/l

Human Health

Both N-nitrosamines and N-nitrosamides exhibit acute toxicity, teratogenicity, mutagenicity and/or carcinogenicity. For most, it is the latter capability which demands consideration in the context of human exposure since the toxicological evidence is such that they must be treated as potential human carcinogens. Thus, nitrosamines are included in the American Conference of Governmental Industrial Hygienists' List of "Industrial Substances Suspect of Carcinogenic Potential for Man." No Threshold Limit Value is given. The guidelines which follow are based upon the assumption that N-nitrosamines are human carcinogens.

Adequate dose-response data to permit an assessment of the carcinogenic risk to man are available from studies involving lifetime exposure of rats or mice to four nitrosamines (N-nitrosodimethylamine, N-nitrosodiethylamine, N-nitrosodi-n-butylamine, and N-nitrosopyrrolidine) in their drinking water or food. These data have been used to derive estimates of the concentrations in water which, if used as the source for man of drinking water and edible fish and shellfish, would increase the risk of a tumor by not more than one in 100,000 individuals exposed for the duration of their lifespan. The method of extrapolation was based on a linear, non-threshold mathematical model. The water criteria numbers given in Table 5 are based upon the tumor incidence, at the organ which is the chemical's principal site of action, in the most sensitive sex, at the lowest dose level which yield a response significantly greater than in the control animals. The actual parameters used are given in Summary of Pertinent Data.

The only nitrosamine for which any data on bioaccumulation in fish or shellfish are available is N-nitrosodiphenylamine. One test in bluegill yielded a maximum bioconcentration factor (BCF) of 217 for the whole fish. Using this, a weighted BCF for all species was calculated to be 500. These values are believed not to be representative for the nitrosamines for which carcinogenicity data are available and another approach has therefore been attempted. A relationship has been described between the BCF and the n-octanol/water partition coefficient, Log BCF=0.76 Log P-0.23. The equation can be used to estimate the BCF for aquatic organisms that contain about 8 percent lipids from the partition coefficient P. The partition coefficients for N-nitrosodimethylamine, N-nitrosodiethylamine, N-nitrosodi-n-butylamine and N-nitrosopyrrolidine are 0.27, 3, 83, and 0.65 respectively.

Values of BCF calculated using this equation are 0.2, 1.4, 17, and 0.42 respectively, for N-nitrosodimethylamine, N-nitrosodiethylamine, N-nitrosodi-n-butylamine, and N-nitrosopyrrolidine, respectively. An adjustment factor of 2.3/8.0=0.2875 can be used to adjust the estimated BCF from the 8.0 percent lipids on which

the equation is based to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish.

The adjusted BCF values are 0.06, 0.39, 4.9, and 0.12 respectively.

Other empirical procedures can be used to estimate BCF's from partition coefficients. The values obtained are of the same order of magnitude.

For purposes of calculating criteria, the estimated BCF's for the methyl, ethyl, butyl, and pyrrolidine compounds are judged to be rough estimates of the bioconcentration potential. As the influence of these values ranges from 5/100 percent to 4 percent of the exposure uptake from fish consumption, for simplicity the assumed BCF for criteria level purposes is zero.

TABLE 5.—*Concentrations in Water Estimated To Induce no More Than One Excess Cancer Per 100,000 Individuals Exposed Over a Lifetime*

Compound	Estimated concentration (μg/l)	Data base
N-Nitrosodimethylamine	0.026	Rats (female) (Druckery, et al. 1967).
N-Nitrosodimethylamine	0.0092	Rats (male?) (Druckery, et al. 1963).
N-Nitrosodi-n-butylamine	0.013	Mice (male) (Bertram and Craig, 1970).
N-Nitrosopyrrolidine	0.11	Rats (mixed sexes) (Preussman, et al. 1977).

The relative carcinogenic potential of N-nitrosodiethylamine (3.20) is exceeded by only that for N-nitrosomethyl-2-chloroethylamine (3.21) and approached by only the values for N-nitroso-methylbenzylamine (3.10) and N-nitrosomethyl-(2,phenylethyl)amine (3.01). Hence, N-nitrosodiethylamine can reasonably be considered to be one of the most carcinogenic nitrosamines. It is therefore appropriate to base the water criterion number for any individual nitrosamine on the number obtained for N-nitrosodiethylamine, *viz*, 9.2 ng/l.

This criterion number has been derived by considering only the excess cancer risk imposed by exposure to contaminated drinking water, fish, and shellfish. However, the average daily intake of preformed nitrosamines from other sources (air, diet, and smoking) is estimated to be in the order of a few micrograms per day. There is an additional and, at the present time, ill-defined contribution to the body burden from the *in vivo* nitrosation of precursors. This contribution has been variously estimated to range from a few micrograms to several hundred micrograms daily. Thus, present evidence suggests that control of exposure to N-nitrosamines should take into account both preformed nitrosamines and their precursors in the environment.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Nitrosamines are suspected of being human carcinogens. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of nitrosamines in water for maximum protection of human health is ZERO.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of nitrosamines corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria[1]			
	0	10^{-7} (μg/l)	10^{-6} (μg/l)	10^{-5} (μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish[2]:				
N-nitrosodimethylamine	0	.000026	.0026	.026
N-nitrosodiethylamine	0	.000092	.00092	.0092
N-nitrosodi-n-butylamine	0	.00013	.0013	.013
N-nitrosopyrrolidine	0	.0011	.011	.11
Consumption of fish and shellfish only:				
N-nitrosodimethylamine	0			
N-nitrosodiethylamine	0			
N-nitrosodi-n-butylamine	0			
N-nitrosopyrrolidine	0			

[1] Calculations by applying a modified "one-hit" extrapolation model described in the methology document to the animal bioassay data presented in summary of pertinent data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately zero percent of Nitrosamine exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of zero. The remaining 100 percent of Nitrosamine exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of nitrosamines, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding nitrosamines concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding nitrosamines concentrations. Because data indicating other sources of nitrosamines exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect in incremental risks associated with the indicated routes only.

Summary of Pertinent Data

Druckery (1967)[1] summarized a series of experiments in which a large series of nitrosamine compounds were given to B-D rats for a lifetime. He found that the incidence of liver tumors increased with daily dose, d, and that the median time when tumors were obsered, t_{50}, was less at higher doses and the relationship between d and t_{50} was $d(t_{50})2.3=k$, where k is a constant equal to 0.81×10^{4}mM/kg/day when t_{50} is expressed in units of days. The extrapolation model used the dose units of mg/kg/day and the time units of fractions of a lifetime. Converting k to these units by using 728 days as the lifetime and a molecular weight of 74 mg/mM gives the following:

$$\frac{k=0.81\times10^{4}\text{mM/kg/day}\times74\text{ mg/mM}=0.30271}{(728)\ 2.3}$$

Therefore the parameters of the dose-response model are:

$n_t/N_t=0.05$
$n_c/N_c=0$
w=0.35 kg
L=728 days
$_{\alpha}n=0.30271$
R=0

The result is that the water concentration should be less than 0.026 micrograms per liter in order to keep the individual lifetime risk below 10^{-5}.

Druckery, et al. (1963)[2] administered diethylnitrosamine to B-D rats via drinking water in nine dose groups ranging from .075 to 14.2 mg/kg/day.

They found that the incidence of liver tumors increased with daily dose, d, and that the median time when tumors were observed, t_{50}, was less at higher doses and the relationship between d and t_{50} was $d(t_{50})^{2.3}=k$, where k is a constant. At a dose of 0.6 mg/kg/day the incidence of tumors reached 50 percent (30 animals with liver tumors out of 60 animals initially) at 355 days. Using a bioaccumulation factor of zero the parameters of the extrapolation model are:

$n_t=30$
$N_t=60$
$nc/N_c=0$
Le=355 days
le=355 days
d=0.6 mg/kg/day
w=0.28 kg
L=730 days
m=2.3 instead of 3 in the standard model
$dt^{m}=0.6$ (3dd/$730^{2.3}$=0.114
R=0

The result is that the water concentration should be less than 0.0092 micrograms per liter in order to keep the individual lifetime risk below 10^{-5}.

Bertram and Crain (1970)[3] administered dibutylnitrosamine via drinking water to C57BL/6 mice at dose levels of about 8 and 30 mg/kg/day until the animals became moribund or died. They found that all of the 179 animals reaching autopsy had tumors of the bladder of esophagus except three, which had tumor induction at either site was the males given 7.6 mg/kg/day, where the mean tumor induction time was 261 days. Assuming a bioaccumulation factor of zero, the parameters of the extrapolation model are:

$n_t/N_t=0.5$
$N_c/n_c=0$
Le=261 days
le=261 days
d=7.6 mg/kg/day
L=728 days
w=.028 kg
R=)

The result is that the water concentration should be less than 0.013 micrograms per liter in order to keep the individual lifetime risk below 10^{-5}.

Preussman, et al. (1977)[4] found a dose-related incidence of hepatocellular carcinomas in Sprague-Dawley rats in a lifetime feeding study at levels of 0.3, 1.0, 3.0, and 10 mg/kg/day. The total tumor incidence was equal to controls at the 0.3 mg/kg/day level, but was 46, 84 and 32 percent at the successively higher doses. Animals at the highest dose had a smaller tumor incidence because of early deaths from pneumonia. At 3 mg/kg/day the incidence of liver tumors was 31/38 whereas the 61 controls had no tumors. With a negligible fish accumulation, the parameters of the dose-response model are:

nt=31
$N_t=38$
$n_c=0$
$N_c=61$
Le=104 weeks
le=104 weeks
d=3 mg/kg/day
w=0.35 kg
L=104 weeks
R=0

The result is that the water concentration should be less than 0.11 micrograms per liter in order to keep the individual lifetime risk below 10^{-5}.

PENTACHLOROPHENOL

Criteria Summary:

Freshwater Aquatic Life

For pentachlorophenol the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 6.2μg/l as a 24-hour average and the concentration should not exceed 14μg/l at any time.

Saltwater Aquatic Life

For pentachlorophenol the criterion to protect saltwater aquatic life as derived using the Guidelines is 3.7μg/l as a 24-hour average and the concentration should not exceed 8.5μg/l at any time.

Human Health

For the protection of human health from the toxic properties of pentachlorophenol ingested through water and through contaminated aquatic organisms, the ambient water quality criterion is determined to be 140μg/l.

Basis for Criteria:

Freshwater Aquatic Life

The absence of chronic toxicity data and the incomplete picture of the effects of pH on the toxicity of PCP render the establishment of a water quality criterion for PCP rather uncertain. A concentration of 1.5μg/l may inhibit fish growth slightly. In addition, complete chlorosis of algae was reported at 7.5μg/l.

No freshwater criterion can be derived for pentachlorophenol using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

Data for pentachlorophenol and saltwater organisms can be used to estimate a criterion.

For pentachlorophenol and saltwater organisms, 0.44 times the Final Acute Value is less than the Final Chronic Value derived from results of a life cycle test with the sheepshead minnow. Therefore, a reasonable estimate of a criterion for pentachlorophenol and freshwater organisms would be 0.44 times the Final Acute Value.

The maximum concentration for pentachlorophenol is the Final Acute Value of 14μg/l and the estimated 24-hour average concentration is 0.44 times the Final Acute Value. A 10 percent reduction in growth of sockeye salmon was observed at a concentration of 3.5μg/l, a concentration slightly lower than the 24-hour average concentration. It is felt that additional data on adverse effects at these concentrations are needed before lowering the criterion.

For pentachlorophenol the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 6.2μg/l as a 24-hour average and the concentration should not exceed 14μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures:

Final Fish Acute Value=25μg/l

Final Invertebrate Acute Value=14μg/l

[1] Druckrey, H., et al. 1967. Organotropic carcinogenic action of 65 different N-nitroso compounds in BD rats. Z. Krebsforsch. 69:103.

[2] Druckrey, H. et al. 1963. Quantitative analysis of the carcinogenic action of diethylnitrosamine. Arzneimittel-Forsch, 13:841.

[3] Bertam, J. S., and A. W. Craig, 1970. Induction of bladder tumours in mice with dibutylnitrosamine. Br. Jour. Cancer, 24:352.

[4] Preussmann, R., et al. 1977. Carcinogenicity of N-nitrosopyrrolidine: dose-response study in rats. Z. Krebsforsch. 90:161.

Final Acute Value=14μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=7.5μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=7.5μg/l
0.44 x Final Acute Value=6.2μg/l

Saltwater Aquatic Life

The maximum concentration of pentachlorophenol is the Final Acute Value of 8.5μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For pentachlorophenol the criterion to protect saltwater aquatic life as derived using the Guidelines is 3.7μg/l as a 24-hour average and the concentration should not exceed 8.5μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.
Final Fish Acute Value=25μg/l
Final Invertebrate Acute Value=8.5μg/l
Final Acute Value=8.5μg/l
Final Fish Chronic Value=9.6μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=290μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=9.6μg/l
0.44×Final Acute Value=3.7μg/l

Human Health

Based on available and cited literature, PCP is not considered to be carcinogenic.

A criterion can be calculated using the data from the chronic toxicity studies. Using a NOEL of 3 mg/kg for low non-phenolic PCP and applying a 0.01 amimal to human uncertainty factor the upper limit for non-occupational daily exposure is 0.03 mg/kg or 2.10 mg/70 kg person.

For the purposes of establishing a water quality criterion, human exposure to PCP is considered to be based on ingestion of 2 liters of water and 18.7 g of fish. The amount of water ingested is approximately 100 times greater than the amount of fish consumed. However, fish bioaccumulate PCP from water by a factor of 58 and thus contain about half as much PCP per gram as water.

With these considerations in mind, the following equation has been established:

$$2L\times X+(0.0187\times 58)\cdot\times X=2.10\text{ mg}$$

Where:

2.10 mg=limit on daily exposure for a 70 mg person (ADI)
2 L=amount of drinking water consumed
0.0187 mg=amount of fish consumed
58=bioaccumulation factor

Solving for X:

$$X=0.68\text{ mg/l}$$

Thus, 1.4 mg of the ADI can be obtained from 2L of drinking water and 0.7 mg from ingested fish.

Present food residues of PCP are reported to be 0 to 10μg/kg and one report of 0.06μg/kg in water. These levels are well below the criterion and total daily general population exposures are less than 1 percent of the calculated maximum value based on toxicologic considerations.

It should be noted that the criterion recommended in this document is based on a NOEL of low non-phenolic PCP, a compound found to be non-carcinogenic at the dosages tested. However, NCI is presently conducting studies on the carcinogenicity of PCP contaminants, hexachloro-p-dioxin, and octachloro-p-dioxin, the results of which are not yet available. The results of these studies should be evaluated before any EPA regulatory standards are established.

SELENIUM

Criteria Summary:

Freshwater Aquatic Life

For selenium the criterion to protect freshwater aquatic life, as derived using procedures other than the guidelines, is 9.7μg/l as a 24-hour average and the concentration should never exceed 22μg/l at any time.

Saltwater Aquatic Life

For selenium the criterion to protect saltwater aquatic life as derived using the Guidelines is 4.4μg/l as a 24-hour average and the concentration should not exceed 10μg/l at any time.

Human Health

For the protection of human health from the toxic properties of selenium ingested through water and through contaminated aquatic organisms, the ambient water criterion is determined to be 10μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

To derive the criterion for selenium, the maximum concentration is the Final Acute Value of 22μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

Summary of Available Data

Final Fish Acute Value=940μg/l
Final Invertebrate Acute Value=22μg/l
Final Acute Value=22μg/l
Final Fish Chronic Value=16μg/l
Final Invertebrate Chronic Value=47μg/l
Final Plant Value=50μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=16μg/l
0.44 × Final Acute Value=9.7μg/l

To derive the criterion for selenium, the maximum concentration is the Final Acute Value of 22μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value.

Saltwater Aquatic Life

To derive the criterion for selenium, the maximum concentration is the Final Acute Value of 10μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations are expressed in terms of selenium.
Final Fish Acute Value=990μg/l
Final Invertebrate Acute Value=10μg/l
Final Acute Value=10μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=26μg/l
Final Plant Value=7,900μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=26μg/l
0.44 × Final Acute Value=4.4μg/l

Human Health

The question of the carcinogenic potential for ingested selenium has been reviewed in recent years by the National Academy of Sciences while studies by the National Cancer Institute have added new but inconclusive evidence to the issue. The Academy states that although the 1962 drinking water standard was recommended at 10μg/l because of evidence that selenium was carcinogenic in animal studies, "a current literature review of animal studies does not support this contention".

An NCI bioassay of selenium disulfide at 100 mg per kilogram (equivalent to 400 ppm of selenium alone) has reported the induction of hepatocellular carcinomas in female mice. This is consistent with an earlier report by Nelson, et al., that seleniferous grains

and ammonium potassium selenide at 10 ppm induced liver tumors in rats. However several inconclusive and negative carcinogenesis studies of selenite and selenate compounds ranging from 2–15 ppm have been reported since Nelson's work.

The carcinogenicity of selenium compounds is a complex issue because: (1) There is evidence that selenates, selenites, and selenides at non-toxic levels inhibit the development of spontaneous tumors, protect against the induction of tumors by known carcinogens, counteract the promotion of tumors in mouse skin initiator-promotor experiments, and inhibit the mutagenic action of chemicals in bacteria; (2) human cancer mortality at several organ sites appears to be negatively correlated with estimated selenium dietary intake and blood selenium levels, according to a tabulation of data from several countries; (3) even at moderate concentrations (5–10 ppm) of selenates and selenites the chronic toxicity is high, and this toxicity interferes with the development of tumors because of early deaths; (4) the aqueous solubility and therefore the availability of different selenium compounds for absorption from the GI tract is markedly variable; (5) low concentrations of selenium (0.01 to 0.1 ppm in the diet) appear to be nutritionally essential; and (6) the reports of the chronic toxicity studies are difficult to compare because of the large number of different selenium compounds studies, the dependence of tumor induction on changes in protein and selenium levels in the diet and the incomplete histopathological examination performed in many of the available studies.

For these reasons it does not seem reasonable to use carcinogenic toxicity and risk as a basis for health criteria without additional research.

Obviously, one of the major factors involved in estimation of the minimum dose of selenium required to produce chronic toxicity in man or animals is the criteria, or definition, of chronic toxicity. The National Research Council has reviewed the literature in an attempt to establish a "no-effect" dose level for selenium and thus arrive at some conclusion concerning the level in water that can be expected to injure man. From this review, they found that the growth rate for rats fed a normal diet was inhibited if exposed to 4 to 5μg/g of selenium in the diet. Only 1μg/g of selenium in the diet was required to reduce growth in rats fed a diet severely deficient in vitamin E. Hadjimarkos has demonstrated in rats that selenium added to drinking water at a level as low as 2.3 mg/l during tooth development increases the incidence of caries. The National Research Council suggests that if histopathologic observations are used as the criteria for chronic toxicity that 1μg/g of selenium in the diet or 1 mg/l if selenium in drinking water may be shown to be sufficient to produce toxicity. However, it is recognized that the physiologic significance of the findings may not be clear, and the same may be said for biochemical parameters indicating the even lower levels can be toxic.

The amount of selenium needed to prevent deficiency diseases in animals is very small; 0.1μg/g in the diet is a nutritional adequate level for most species. Such a level translates into a human requirement of about 60 to 120 micrograms per day depending on the biologic availability in the diet, a person's physiologic status with regard to other nutrients, and other factors.

It is estimated that on the average, adults intake roughly 130 to 150μg of selenium per day from food. Levander has estimated that an average six month old infant consumes 28μg of selenium per day from food.

The uneven distribution of selenium in the soils of the United States could conceivably cause persons living in low-selenium areas and consuming only locally produced foods to develop a low-selenium state, just as some who live in high-selenium areas may ingest excess selenium. However most nutritional authorities agree that there is currently no evidence of selenium deficiency in human populations in the United States, probably because of interregional food shipment that characterizes our present-day food supply.

Hence, there is no need to use water as a vehicle for supplementing the diets of the general population.

In consideration of the probable importance selenium plays in the human diet, and the varied but definite exposure potential from food intake, drinking water and other sources, the strategy for identifying a criterion level for ambient waters must be based on minimizing the likelihood of contributing a sufficient amount of selenium that would increase an average total exposure above a selected toxic level.

The growth inhibition with vitamin E deficiency would be the candidate of first choice for toxicity effect and extrapolation into human effects. However, the vitamin E circumstance would be a special situation for the average population and therefore the increased incidence of dental caries at 2.3 mg/l becomes the targeted effect for extrapolation to humans.

If it is assumed that rats consume 10 percent of their body weight per day during their growth period, the toxic effect (incidence of dental caries) is demonstrated at levels of selenium as low as 16 mg selenium intake per day.

$$2.3 \frac{mg}{l} \text{ selenium} = 2.3 \frac{mg}{kg} \text{ feed}$$

Assuming 300gr rat;

$$\text{feed intake} = 2.3 \frac{mg}{kg} \times 10\% \text{ (300gr)} = \frac{69 \times 10^{-3} \text{mg Se}}{\text{day}}$$

$$\text{animal dose} = \frac{69 \times 10^{-3} \text{ mg}}{\frac{\text{day}}{300\text{gr}}} = \frac{0.23 \text{ mg Se}}{\text{kg body wt}}$$

$$\text{equivalent human dose} = \frac{0.23 \text{ mg Se}}{\text{kg body wt}} \times 70 \text{ kg man} = 16.1 \text{ mg Se}$$

Thus, the equivalent human dose for incidence of dental caries is 16.1

$$\frac{\text{mg Se}}{\text{day}}$$

For comparison purposes a similar calculation for the growth inhibition under vitamin E deficiency is

$$\frac{7 \text{ mg Se}}{\text{day}}$$

Summary of Pertinent Data

In summary, the minimum toxic daily dose is 16,100 micrograms and the average daily dietary intake is 130 to 150 micrograms leaving a difference of 15,950 micrograms. Populations living in seleniferous areas may be exposed to much higher levels of selenium both in the food and water. Since little is known concerning the minimum toxic dose in humans and there is uncertainty about the carcinogenic potential of Se, it does not seem reasonable to permit the level in water to be more than ten to twenty percent of the dietary level. If the maximum water contribution is set at 13 to 30.0 micrograms per day, the total level (dietary and water) will be well below the estimated minimum toxic dose. Assuming that the average individual con-

sumes 2 liters of drinking water per day, 18.7 grams of fish, and that the bioaccumulation factor for fish is 18, the estimated level for water is calculated as follows:

$$\text{Criterion Level} = \frac{13}{2 + (0.0187)\ 18} = 5.56\ \mu g/\text{liter}$$

$$\text{or} = \frac{30.0}{2 + (0.0187)\ 18} = 12.84\ \mu g/\text{liter}$$

Based on these calculations it appears that the U.S. Environmental Protection Agency Drinking Water Standard of 10μg/liter is probably an appropriate ambient criterion level to protect the health of the U.S. population.

SILVER

Criteria Summary:

Freshwater Aquatic Life

For silver, the criterion to protect freshwater aquatic life derived using the Guidelines, is 0.0090μg/1 as a 24-hour average and the concentration should not exceed 1.9μg/1 at any time.

Saltwater Aquatic Life

For silver, the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.26μg/1 as a 24-hour average and the concentration should not exceed 0.58μg/1 at any time.

Human Health

For silver, the criterion to protect human health from the toxic properties of silver ingested through water and through contaminated aquatic organisms is 10μg/1.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of silver is the Final Acute Value of 1.9μg/1 and the 24-hour average concentration is the Final Chronic Value of 0.0090μg/1. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For silver the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0090μg/1 as a 24-hour average and the concentration should not exceed 1.9μg/1 at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of silver.

Final Fish Acute Value=5.6μg/l

Final Invertebrate Acute Value=1.9μg/l

Final Acute Value= 1.9μg/1

Final Fish Chronic Value=0.0090μg/l

Final Invertebrate Chronic Value=not available

Final Plant Value=10μg/1

Residue Limited Toxicant Concentration=not available

Final Chronic Value=0.0090μg/l

0.44×Final Acute Value=0.84μg/l

Saltwater Aquatic Life

The maximum concentration of silver is the Final Acute Value of 0.58μg/1 and the 24-hour average concentration is 0.44 times the Final Acute Value of 0.26μg/1. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For silver, the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.26μg/1 as a 24-hour average and the concentration should not exceed 0.58μg/1 at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of silver.

Final Fish Acute Value=not available

Final Invertebrate Acute Value=0.58μg/1

Final Acute Value= 0.58μg/1

Final Fish Chronic Value= not available

Final Invertebrate Chronic Value= 3.6μg/1

Final Plant Value=130μg/1

Residue Limited Toxicant Concen>tration=not available

Final Chronic Value=3.6μg/1

0.44×Final Acute Value=0.26μg/1

Human Health

None of the carcinogenicity studies mentioned in the criteria document are acceptable for extrapolation to drinking water by use of the linear, non-threshold model (see Methodology Document). No study demonstrating carcinogenicity of silver has met all of the criteria described in 40 CFR 162.11 (a) ii, A or 43 FR 163.83-2bc regarding appropriate route, chemical form, number of animals, histologic examination of organs and all obvious lesions, concurrently run control group, etc.

Data on Human Effects: Although numerous references to the health effects of silver on humans are available, relatively little toxicological or epidemiological data have been reported in the past 30 years. The primary health effect reported is argyria, the unsightly blue-gray discoloration of the skin (and other organs) that develops after repeated exposures to silver compounds. (It is rarely seen today). The current drinking water standard of 50 μg/l was designed to protect against argyria.

Extrapolations from Animal Data: In ten experiments on chronic ingestion by a limited number of rats (rabbits included in one study) of drinking water containing 50 to 20,000 μg/l silver ions, effects were not observed in rats ingesting silver at less than 400 μg/l. However, in four studies, some physiological effect was noted at 400 or 500 μg/l of silver. Thus, for the purpose of developing a criterion for silver based on animal studies of reasonable quality, the following calculation may be made:

$$\frac{(0.2\ mg/1)\ (0.035\ 1/day\ *)}{0.3\ kg**} = 0.023\ mg/kg/day$$

0.023 mg/kg/day×70 kg/adult human male=1.6 mg/day

* Estimated volume of water consumed by rats.

** Estimated weight of one rat.

A safety factor of 10 to 100 is indicated here, based on several factors:

The National Academy of Sciencies guidelines:

Some valid experimental results are available for prolonged human ingestion with no indication of carcinogenicity, but data are less than complete.

The water consumption rate for rats is considerably higher than that for humans on equivalent body weight basis.

The retention rate of silver in humans versus that in rats is uncertain.

While silver had not been found to be carcinogenic by normal intake routes some evidence exists that it may have carcinogenic activity when implanted as a solid or have activity as a promoter for other carcinogens.

Application of a safety factor of 100 yields a concentration of 8 μg/l, i.e.

$$\frac{1.6\ mg/day}{(100)\ 2\ L} = \frac{0.016\ mg/day}{2L} = 0.008\ mg/l = 8\ \mu g/l$$

Because of the inherent uncertainties in such a calculation, a value of 10 μg/l silver in water is chosen as the criterion level for protection of human health.

2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN

Criteria Summary:

Freshwater Aquatic Life

For freshwater aquatic life, no criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for 2,3,7,8-tetrachlorodibenzo-p-dioxin can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to TCDD through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of TCDD estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 4.55×10^{-7} μg/l, 4.55×10^{-8} μg/l, and 4.55×10^{-9} μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

Although few data are available for this compound, sufficient information exists to indicate a potential high environmental hazard. A variety of aquatic organisms bioconcentrated 2,3,7,8-tetrachlorodibenzo-p-dioxin to 20,000 times or more. When coho salmon were exposed for 96 hours and placed in uncontaminated water for observation over a 60-day period, there was 12 percent mortality of those fish exposed to 0.000056 μg/l.

No freshwater criterion can be derived for 2,3,7,8-tetrachlorodibenzo-p-dioxin using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

Final Fish Acute Value=not available
Final Inverterbrate Acute Value=not available
Final Acute Value=not available
Final Chronic Value=not available
Final Invertebrate Chronic Value=not available
Fianl Plant Value=not available
Residue Limited Toxicant Concentration =not available
Final Chronic Value=not available
0.44×Final Acute Value=not available

Saltwater Aquatic Life

No saltwater criterion can be derived for 2,3,7,8-tetrachlorodibenzo-p-dioxin using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

None available.

Human Health

Basis and Derivation of Criteria. TCDD is an extremely toxic compound exhibiting acute, subchronic and chronic effects in animals and humans. The liver appears to be the target organ of acute exposure. Retention of TCDD by the liver indicates that it apparently undergoes little or no metabolism.

Acute effects of exposure include chloracne, prophyria cutanea tarda, hepatotoxicity, psychological alterations, wieght loss, thymic atrophy, thromboctopenia, suppression of cellular immunity and death. TCDD is teratogenic and fetotoxic. Oral exposure of pregnant rats to 0.125 to 2.0μg TCDD/kg/day produced fetal mortality, fetal intestinal hemorrhage and both early and late resorptions. There was found an increased incidence of cleft palate when pregnant mice were given TCDD doses of 1.0μg/kg/day for 10 days during gestation. TCDD has been shown to be mutagenic in three bacterial systems and a potent inducer of hepatic and renal micosomal drug metabolizing enzmes.

The carcinogenic potential of tetrachlorodibenzo-p-dioxin has been established by the findings of two feeding studies. One study found that Spargue-Dawley rats fed dose levels of 5 ppt to ppb TCDD had a significant excess of tumors in TCDD treated rats as compared to the controls. Another feeding study, conducted by Kociba, et al., (In Press) [1] using the same strain of rats given 0.1, 0.01, 0.001 μg TCDD/kg/day, induced a statistically significant excess of hepatocellular carcinoma in treated rats. Based on these two studies, tetrachlorodibenzo-p-dioxin is likely to be a human caroinogen.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." TCDD is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of TCDD in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of TCDD corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5} 10^{-6} or 10^{-7} as shown in the following table.

[1] Kociba, et al. In Press. Toxic and App. Phar.

Exposure assumptions (per day)	Risk levels and corresponding criteria[1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liter of drinking water and consumption of 18.7 grams fish and shellfish[2]	0	4.55×10^{-9}	4.55×10^{-8}	4.55×10^{-7}
Consumption of fish and shellfish only	0	4.63×10^{-9}	$4.6310\times^{-8}$	
		$44.6310\times^{7}$		

[1] Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Appendix I of the document. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately 98 percent of the TCDD exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 5,800-fold. The remaining 2 percent of TCDD exposure results from drinking water.

Concentration levels were derived assiming a lifetime exposure to various amounts of TCDD, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding TCDD concentrations and, (2) occurring solely from comsumption of aquatic life grown in the waters containing the corresponding TCDD concentrations. Because data indicating other sources of TCDD exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Summary of Pertinent Data

The Kociba, et al. study of Sprague-Dawley rats in which dioxin was added to the diet at a concentration of 0.1μg/kg/day for 2 years resulted in hepatocellular carcinoma in 11 of 49 treated females whereas only 1 of 86 controls had hepatocellular carcioma. Using a bioaccumulation factor 5,800 the parameters of the extrapolation model are:

$n_t=11$
$N_t=49$
$n_c=1$
$N_c=86$
Le=24 months
le=24 months
$d=10^{-4}$mg/kg/day
w=0.37 kg
L=24 months
R=5,800

The result is that the water concentration should be less than 4.55×10^{-7} micrograms per liter in order to keep the individual lifetime risk below 10^{-5}.

TETRACHLOROETHYLENE

Criteria Summary:

Freshwater Aquatic Life

For tetrachloroethylene, the criterion to protect freshwater aquatic life, as derived using procedures other than the Guidelines, is 310μg/l as a 24-hour average and the concentration should not exceed 700μg/l at any time.

Saltwater Aquatic Life

For tetrachloroethylene the criterion to protect saltwater aquatic life as derived using the Guidelines is 79μg/l as a 24-hour average and the concentration should not exceed 180μg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to tetrachloroethylene through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of tetrachloroethylene estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 2.0μg/l, 0.20μg/l, and 0.020μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for tetrachloroethylene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available.

However, results obtained with tetrachloroethylene and trichloroethylene and saltwater and freshwater organisms respectively indicate how a criterion may be estimated.

For tetrachloroethylene and saltwater organisms and for trichloroethylene and freshwater organisms the Final Chronic Value based on data for invertebrate species is greater than 0.44 times the Final Acute Value. Therefore, it seems reasonable to estimate a criterion for tetrachloroethylene and freshwater organisms using 0.44 times the final Acute Value.

To estimate a criterion for tetrachloroethylene, the maximum concentration is the Final Acute Value of 700μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For tetrachloroethylene the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 310μg/l as a 24-hour average and the concentration should never exceed 700μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=2,600μg/l
Final Invertebrate Acute Value=700μg/l
Final Acute Value=700μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=greater than 820,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=greater than 820,000μg/l
0.44×Final Acute Value=310μg/l

Saltwater Aquatic Life

The maximum concentration is the Final acute Value of 180μg/l and the 24-hour average concentration is 0.44 times the Final Acute Value. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

For tetrachloroethylene the criterion to protect saltwater aquatic life as derived using the Guidelines is 79μg/l as a 24-hour average and the concentration should never exceed 180μg/l at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=not available
Final Invertebrate Acute Value=180μg/l
Final Acute Value=180μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=88μg/l
Final Plant Value=11,000μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=88μg/l
0.44×Final Acute Value=79μg/l

Human Health

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Tetrachloroethylene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of tetrachloroethylene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of tetrachloroethylene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria [1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish [2]	0	0.020	0.20	2.0
Consumption of fish and shellfish only	0	0.040	0.40	4.0

[1] Calculations by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Summary of Pertinent Data.

Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately 51 percent of the tetrachloroethylene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 110-fold. The remaining 49 percent of tetrachloroethylene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of tetrachloroethylene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding tetrachloroethylene concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding tetrachloroethylene concentrations. Because data indicating other sources of tetrachloroethylene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Summary of Pertinent Data

Tetrachloroethylene administered by gavage to mice caused hepatocellular carcinomas in both males and females in the NCI [1] bioassay at both the high and low dose levels. The females were treated at 772 and 386 mg/kg five times per week for 78 weeks and held until 90 weeks for observation. In females of the high dose group the lifetime probability of dying of hepatocellular carcinoma was 0.938, whereas the matched vehicle and matched untreated controls had an incidence of hepatocellular carcinoma indistinguishable from that of pooled controls, which was 6/196. The lifetime probability given in the NCI report is used for the water criteria documents rather than the actual incidence because a correction is needed for the excess early deaths in the treated groups due to kidney toxicity. With a fish bioaccumulation factor of 110, the parameters of the extrapolation model are:

$n_i/N_i = 0.938$
$n_c = 6$
$N_c = 196$
Le = 90 weeks
le = 78 weeks
d = 772 x 5/7 = 551 mg/kg/day
w = .026 kg
L = 90 weeks
R = 110

The result is that the water concentration should be less than 2.0 micrograms per liter (2.04 μg/l) in order to keep the individual lifetime risk below 10^{-5}.

[1] National Cancer Institute. 1976. Carcinogenesis bioassay of trichloroethylene. CAS No. 79-01-6, NCI C8-TR-2 DHEW Publication No. (NIH) 76-802.

THALLIUM

Criteria Summary:

Freshwater Aquatic Life

For freshwater aquatic life, no criterion for thallium can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for thallium can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the protection of human health from the toxic properties of thallium ingested through water and contaminated aquatic organisms, the ambient water criterion is 4 μg/l.

Basis for the Criteria:

Freshwater Aquatic Life

No freshwater criterion can be derived for thallium using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of thallium.

Final Fish Acute Value=860 μg/l
Final Invertebrate Acute Value=88 μg/l
Final Acute Value=88 μg/l
Final Fish Chronic Value=less than 6.0 μg/l
Final Invertebrate Chronic Value=not available
Final Plant Value=100 μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=less than 6.0 μg/l
0.44×Final Acute Value=39 μg/l

Saltwater Aquatic Life

No saltwater criterion can be derived for thallium using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures. All concentrations herein are expressed in terms of thallium.

Final Fish Acute Value=3,300 μg/l
Final Invertebrate Acute Value=37 μg/l
Final Acute Value=37 μg/l
Final Fish Chronic Value=not available
Final Invertebrate Chronic Value=not available
Final Plant Value=4,100 μg/l
Residue Limited Toxicant Concentration=not available
Final Chronic Value=4,100 μg/l
0.44×Final Acute Value=16 μg/l

Human Health

The proposed criterion for thallium in water is derived from (1) estimated least toxic level on chronic intake in man (2) introduction of a margin of safety and (3) relative contribution of water and other media to total daily intake in the general population.

In estimating the least toxic level of intake, the effect to which man is most sensitive probably is alcopecia. Loss of scalp hair in man and of body fur in animals seems to occur at somewhat lower levels of intake than any other known effects. This is not so clearly the case in adults as in chil-

dren and animals. There is, however, no great difference between the acute or chronic dose causing alopecia and the dose causing neurologic effects. The least daily amount of thallium which, when taken for a lifetime, will cause alopecia can only be estimated on the basis of sub-chronic animal exposure data combined with some kinetic considerations. It is estimated that the least toxic sub-chronic level of intake in rats was 1.6 mg Tl/kg/d. Alopecia occurred in 2 weeks as a result of the administration of thallium at 12 ppm in the diet. In the following the average weight of rats is derived from inspection of the authors' report; the average food was assumed to be 10 g at that weight:

(1) least toxic dietary level=15 ppm thallous acetate=12 ppm thallium (12 μg/g)
(2) average weight of rats=.075 kg
(3) average diet consumption=10 g/d (12 μg/g) (10g)=240μg Tl/d/.075 kg=1.6 mg/kg/d

In spite of continuous intake for 105 days, animals receiving a modestly lower level (one-third) showed no alopecia or other effects. At the least toxic dose level effects occurred within two weeks or they did not occur with continued intake. This is consistent with the rapid turnover of thallium in rats and the consequently rapid attainment of a steady state level of thallium in the body. Within two weeks, a steady state is virtually achieved since 14 days represents more than three half-lives for thallium clearance from the body. Thus, steady state for input vs output:

$$A = \frac{1.6\ \text{mg/kg/d}}{.18\ \text{day}^{-1}};$$

$$A = 8.9\ \text{mg/kg}$$

where:

A=amount in 1 kg body weight
k=constant for rate of excretion

At 14 days

$$A = \frac{1.6\ \text{mg/kg/d}}{0.18\ \text{d}^{-1}} \cdot (1-e^{-0.17\ \cdot\ 14})$$

$$A = \frac{1.6}{.18} \cdot (1-.09)$$

A=8.1 mg/kg (compared to 8.9 above)

Extrapolation of this minimal toxic level of 1.6 mg/kg/d to man requires one assumption, that man and rat are about equally sensitive to the toxic effects of thallium. This seems reasonable. A comparison of minimal acute lethal doses is possible; 13–20 mg/kg in rats and 8–10 mg/kg in man. However, in order for man to attain the same toxic level in the body as the rat, the required intake is much smaller because the turnover of thallium in the body is much slower (k=0.18 in the rat vs k=0.023 in man). Thus, in man, the dose required to attain a minimally toxic steady state whole body concentration of thallium would be only 0.20 mg/kg/d from:

$$\frac{k\ (\text{man})}{k\ (\text{rat})} = \frac{AD\ (\text{man})}{A_D\ (\text{rat})}$$

where: A_D = mg Tl/kg/d

= 1.6 mg/kg (rat)

Because of the tenuous nature of the data on which these calculations are based, it must be accepted that the minimal toxic level of chronic exposure may be lower than estimated here. Even assuming that the minimal toxic dose is actually lower than estimated, the spread between toxic intake and man's current level of intake is considerable. It is estimated that the usual input from drinking water, food and air is no more than 6μg/d for an adult weighing 70 kg. This is in contrast to a minimal toxic level of 15.4 mg/day for a person weighing 70 kg. The safety factor is thus approximately 2500

$$\left(\frac{15{,}400\ \mu\text{g/d}}{6.0\ \mu\text{g/d}}\right)$$

So far as a safe level of thallium in drinking water is concerned, there does not seem to be any reasonable possibility that even the most thallium-polluted waters would have a toxic effect. In the worst case identified by Zitko et al. the concentration of thallium was 88μg/1. Assuming that this were a human water supply, the daily input at 2 1. per day would be only 176μg Tl, 0.011 times the minimally toxic input calculated in this document.

The great difference between estimated minimally toxic exposures and current total exposure in the general population is reassuring. One cannot be totally sanguine, however, since there is a paucity of chronic data, including mutagenicity, teratogenicity and carcinogenicity. For that reason it seems prudent to keep levels of exposure at or below their present levels. From the data available, it would seem that few if any public water supplies would ever contain more than 4μg/1. This seems like a reasonable standard which would protect against gross excursions beyond the usual range of thallium in water, which appears to be of the order 0.1–1μg/1. This also provides a safety factor of three orders of magnitude–10^3. This is in agreement with well—accepted guidelines of the NAS for calculating a safety factor which is used in the case of compounds where there are: "No long-term or acute human data. Scanty results on experimental animals. No indication of carcinogenicity."

Consumption of 2 liters of water per day and 18.7 grams of fish and shellfish products/day with an average bioconcentration factor of 61 from ambient waters containing 4 μg/1 of thallium results in an intake of 12.56μg Tl/day, compared to the estimated minimal toxic dose of 15,400μg/d.

In summary form, the dose-response scale for man is estimated to be as follows:

Dose	
8–10 mg/kg	minimally lethal single dose
220 μg/kg/d	minimally toxic dose over a lifetime
1000μg/kg/d	category 3 safety factor recommended by NAS according to available data
4μg/1. H_2O	recommended standard
20μg/70kg/d	thallium consumption @ 10μg/1
1μg/1	probable limit for >99 percent of U.S. tap waters
≤ 1μg/d	probable current level of daily adult thallium comsumption from drinking water
15.4 mg/d	acceptable total daily intake of thallium from air, water, and food

TRICHLOROETHYLENE

Criteria Summary:

Freshwater Aquatic Life

For trichloroethylene the criterion to protect freshwater aquatic life (as derived using the Guidelines), is 1,500 μg/1 as a 24-hour average and the concentration should not exceed 3,400 μg/1 at any time.

Saltwater Aquatic Life

For saltwater aquatic life, no criterion for trichloroethylene can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to trichloroethylene through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of trichloroethylene estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding crite-

ria of 21μg/1, 2.1μg/1, and 0.21μg/1, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

The maximum concentration of trichloroethylene is the Final Acute Value of 3,400μg/1 and the 24-hour average concentration is the Final Chronic Value of 1,500μg/1. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

Criterion: For trichloroethylene the criterion to protect freshwater aquatic life as derived using the Guidelines is 1,500 μg/1 as 24-hour average and the concentration should not exceed 3,400 μg/1 at any time.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=7,900μg/1

Final Inverterbrate Acute Value=3,400μg/1

Final Acute Value=3,400μg/1

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=greater than 2,000μg/1

Final Plant Value=not available

Residue Limited Toxicant Concentration=not available

Final Chronic Value=greater than 2,000μg/1

0.44×Final Acute Value=1,500 μg/1

Saltwater Aquatic Life

No saltwater criterion can be derived for trichloroethylene using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value=not available

Final Invertebrate Acute Value=not available

Final Acute Value=not available

Final Fish Chronic Value=not available

Final Invertebrate Chronic Value=not available

Final Plant Value=not available

Residue Limited Toxicant Concentration=not available

Final Chronic Value=not available

0.44×Final Acute Value=not available

Human Health

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Trichloroethylene is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of trichloroethylene in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of trichloroethylene corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or 10^{-7} as shown in the table below.

Exposure assumption (per day)	Risk levels and corresponding criteria[1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish[2]	0	0.21	2.1	21
Consumption of fish and shellfish only	0	0.78	7.8	78

[1] Calculations by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Approximately 27 percent of the trichloroethylene exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 39-fold. The remaining 73 percent of trichloroethylene exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of trichloroethylene, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding trichloroethylene concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding trichloroethylene concentrations. Because data indicating other sources of trichloroethylene exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

Summary of Pertinent Data

The NCI[1] bioassay with male mice at an average dose, administered by stomach tube of 1,169 mg/kg administered five times per week for 78 weeks is used. The experiment was terminated after 90 weeks. In matched control animals the incidence of hepatocellular carcinoma was 1/20 and in treated animals it was 28/50. The fish bioaccumulation factor is 39. The parameters of the extrapolation model are:

nt=26
NT=50
nc=1
NC=20
Le=90 weeks
le=78 weeks
d=1169×5/7=835 mg/kg/day
w=0.034 kg
L=90 weeks
B=39

The result is that the water concentration should be less than 21μg/1 (21.47μg/1) in order to keep the individual lifetime risk below 10^{-5}.

[1] National Cancer Institute, 1976. Carcinogenesis bioassay of trichloroethylene CAS No. 79-01-6, NCI-01-IB-2.

VINYL CHLORIDE

Criteria Summary:

Freshwater Aquatic Life

No freshwater criterion can be derived for vinyl chloride using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Saltwater Aquatic Life

No saltwater criterion can be derived for vinyl chloride using the Guidelines

because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to vinyl chlorides through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of vinyl chloride estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 517 μg/l, 51.7 μg/l, and 5.17 μg/l, respectively.

Basis for the Criteria:

Freshwater Aquatic Life

No criteria have been developed.

Summary of Available Data

No data available.

Saltwater Aquatic Life

No criteria have been developed.

Summary of Available Data

No data available.

Human Health

Vinyl chloride is a well-known human and animal carcinogen. Several occupational epidemiology studies in highly exposed workers have reported excess rates of liver angiosarcoma and tumors at other organ sites. Animal experiments using both inhalation and oral routes of exposure have also induced liver angiosarcoma.

The recommended water quality criterion is calculated using the tumor incidence data from chronic rat inhalation studies. The validity of these incidence rates for humans was established by evaluating the cancer incidence in workers after accounting for their exposure.

Under the Consent Decree in *NRDC v. Train*, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities." Vinyl Chloride is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of vinyl chloride in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of vinyl chloride corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the FEDERAL REGISTER notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6} or 10^{-7} as shown in the table below.

Exposure assumptions (per day)	Risk levels and corresponding criteria[1]			
	0	10^{-7}	10^{-6}	10^{-5}
		(μg/l)	(μg/l)	(μg/l)
2 liters of drinking water and consumption of 18.7 grams fish and shellfish[2]	0	5.17	51.7	517
Consumption of fish and shellfish only	0	260	2600	26,000

[1] Calculated by applying a modified "one-hit" extrapolation model to the animal bioassay and human epidemiological data presented in Summary of Pertinent Data. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

[2] Two percent of the vinyl chloride exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 1.9 fold. The remaining 98 percent of vinyl chloride exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of vinyl chloride, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding vinyl chloride concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding vinyl chloride concentrations.

Although total exposure information for vinyl chloride is discussed and an estimate of the contributions from other sources of exposure can be made, this data will not be factored into ambient water quality criteria formulation until additional analysis can be made. The criteria presented, therefore, assume an incremental risk from ambient water exposure only.

Summary of Pertinent Data

In a previous report on risks to vinyl chloride in the ambient air (Kuzmack and McGaughy, 1975)[1] the rat inhalation experiments of Maltoni and Lefemine (1975)[2] were combined with occupational epidemiology studies to estimate risks to inhaled vinyl chloride. The result was that a continuous exposure of 17 ppb of vinyl chloride results in a lifetime risk of 10^{-5}. On the assumptions that the same daily intake of vinyl chloride via 2 liters of drinking water produces the same risk, and that fish bioaccumulative vinyl chloride to a small degree (BCF=1.9), the following calculation is used to find the water concentration giving a lifetime risk to 10^{-5}.

Intake of vinyl chloride via air is:

$$24\ m^3/day \times 17ppb \times (1\mu g/m^3/0.387ppb) = 1.054 \times 10^3 \mu g/day.$$

If this intake comes from 2 liters of water and ingesting 18.7 grams per day of fish and shellfish products, the ambient water concentration would have to be

$$1.054\ mg/kg/day\ 2 + 1.9(0.0187) = 0.517\ mg/l.$$

[1] Kuzmack, A. M., and R. E. McGaughy. 1975. Quantitative risk assessment for community exposure to vinyl chloride. Environ. Prot. Agency Rep. Dec. 5.

[2] Maltoni, C., and G. Lefemine. 1975. Carcinogenicity assays of vinyl chloride: current results. Ann. N.Y. Acad, Sci. 246:195.

APPENDIX B—GUIDELINES FOR DERIVING WATER QUALITY CRITERIA FOR THE PROTECTION OF AQUATIC LIFE AND ITS USES

FEBRUARY 15, 1979.

INTRODUCTION

This version of the Guidelines provides clarifications, additional details, and technical and editorial changes in the version published in the FEDERAL REGISTER (43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)). The purpose of publising this version is to make available the one that was used in the preparation of the water quality

criteria for aquatic life to help people understand the derivation of the criteria. (For some substances, however, available data from chronic animal studies (see Section XIII B) were not obtained in time for use in the criteria issued today.) The Glossary and the Tables that were published along with the Guidelines in the FEDERAL REGISTER are not reproduced here since they have not been changed. The content of this version does not reflect in any way what will be the Agency response to the comments received on the previously published version.

The Guidelines assume that water quality criteria for aquatic life should protect both the presence and uses of aquatic organisms. Since some substances may be more toxic in fresh water than in salt water, or vice versa, separate water quality criteria are derived for freshwater and saltwater organisms for each substance. However, for some chemicals sufficient data were not available to derive one or both of the criteria using the Guidelines. The Guidelines are intended to describe an objective, consistent, and apropriate way of using the available pertinent information to derive such criteria. The Guideline should not be interpreted as implying that the various ways of obtaining test results, such as static vs. flow-through or measured vs. estimated bioconcentration factors, are equally good.

Section I. Identify needed criteria

A. Usually the substance of concern can be easily classified as either ionizable or non-ionizable.

1. Separate criteria should usually be derived for each individual non-ionizable chemical, except possibly for (a) a compound and one or more of its metabolites and degradation products, or (b) structurally similar compounds that only differ in the number and location of atoms of a specific halogen, only exist as commercial mixtures of the various compounds, are difficult to measure individually, and apparently have similar chemical, biological, and toxicological properties.

For an ionizable chemical, one criterion should usually be derived for all forms that are in chemical equilibrium. Separate criteria should usually be derived for each different form, e.g., valence state or bonding structure, that is not in chemical equilibrium with another chemical for which a criterion has been or is being derived.

B. Based on information on chemical, biological and toxicological properties, determine for which substances criteria are needed.

C. For each substance, determine if criteria are needed for both fresh and salt water. If both criteria are needed, all of the following must be completed once for fresh water and once for salt water.

Section II. Data base

A. Collect all available data on the toxicity of the substance to fish, aquatic invertebrates, and aquatic plants and on the bioconcentration of the substance by aquatic organisms.

B. Discard all data that are not either (1) published or (2) available in manuscript form and obtained using standard test procedures.

C. Discard all data obtained using brine shrimp.

D. Discard data that were not obtained using species resident in North America, Hawaii, or Puerto Rico. Resident North American species of fish are defined as those listed in "A List of Common and Scientific Names of Fishes from the United States and Canada", 3rd ed., Special Publication No. 6, American Fisheries Society, Washington, D.C., 1970.

E. Discard questionable data. For example, discard data obtained using organisms that were previously exposed to significant concentrations of the test material. Discard data from tests for which there was no control treatment, in which control mortality was unacceptably high, or in which distilled or deionized water was used as the dilution water.

Section III. Fish acute values

A. Use the following kinds of data on toxicity to fish (times are ±3 hours):

1. 24-, 48-, 72-, and 96-hr LC50 values.

2. 24-, 48-, 72-, and 96-hr EC50 values based on immobilization.

B. If values are available from one test for more than one of the specified time periods, use only the one for the longest duration. For use of comparable values for times other than those listed above, see Section XIV.

C. Multiply all values based on unmeasured concentrations by an adjustment factor of 0.77 to simulate results based on measured concentrations (a).[1]

D. Multiply all 24-, 48-, and 72-hr values by adjustment factors of 0.66, 0.81, and 0.92, respectively, to simulate 96-hr values (b).

E. Multiply all values from static and renewal tests by an adjustment factor of 0.71 to simulate values from flow-through tests (c).

Section IV. Invertebrate acute values

A. Use the following kinds of data on toxicity to invertebrates (times are ±3 hours):

1. 48-hr LC50 values for daphnids and other cladocerans, midge larvae, and embryos and larvae of barnacles and bivalve molluscs.

2. 48-hr EC50 values based on abnormal development of embryos and larvae of barnacles and bivalve molluscs.

3. 48-hr EC50 values based on immobilization of daphnids and midge larvae.

4. 96-hr EC50 values based on decreased shell deposition for oysters.

5. 24-, 48-, 72-, and 96-hr EC50 values based on loss of equilibrium for shrimp and crabs.

6. 24-, 48-, 72-, and 96-hr EC50 values based on immobilization for invertebrate species not named above.

B. If values are available from one test for more than one of the specified time periods, use only the one for the longest duration. For use of comparable values for times other than those listed above, see Section XIV.

C. Multiply all values based on unmeasured concentrations by an adjustment factor of 0.77 to simulate results based on measured concentrations (a).

D. Multiply all 24-, 48-, and 72-hr values from steps A5 and A6 by adjustment factors of 0.26, 0.43, and 0.61, respectively, to simulate 96-hr values (h). Do not adjust the 48-hr values from steps A1, A2, and A3.

E. Multiply all values from static and renewal tests by an adjustment factor of 1.1 to simulate values from flow-through tests (i).

Section V. Fish chronic values

A. Chronic values are calculated as the geometric mean of the limits on the Maximum Acceptable Toxicant Concentration (MATC) obtained from a life-cycle test or a partial life-cycle test, or one-half the geometric mean of the limits obtained from an embryo-larval test (e).

NOTE.—Some authors report "MATC limits" that are not MATC limits as defined in the Glossary.

Section VI. Invertebrate chronic values

A. Chronic values are calculated as the geometric mean of the MATC limits obtained from a life-cycle test or a partial life-cycle test.

NOTE.—Some authors report "MATC limits" that are not MATC limits as defined in the Glossary.

Section VII. Final values related to water quality

A. If the toxicity of the substance is affected by a water quality characteristic such as hardness for freshwater organisms or salinity for saltwater organisms, the criterion for that substance in that water should be related to that water quality characteristic. Since data of the right kind may not be available to determine whether such a statistically significant relationship exists for both acute and chronic toxicity to both fish and invertebrates, extrapolations from one species to another, assumptions, and judgments

[1] Small letters in parentheses refer to the footnotes appended to the Guidelines.

may have to be used instead of statistical tests.

B. Deriving a relationship (do separately for fish acute values, invertebrate acute values, fish chronic values, and invertebrate chronic values).

1. For each species for which comparable toxicity values are available at two or more different values of the water quality characteristic, perform a least squares regression of the natural logarithms of the toxicity values (adjusted when necessary) on the natural logarithms of the water quality characteristic values. If there are three or more values of the water quality characteristic, test the significance of the relationship using a regression F-test.

2. Determine whether or not each slope is meaningful, taking into account not only the results of the regression F-test, but also the range and number of values of the water quality characteristic tested. For example, a slope from a statistically significant regression may be of limited value if it is based only on data for a narrow range of the water quality characteristic. On the other hand, even though a regression based on only two data points can not be tested for statistical significance, a slope based on a line drawn between only two data points may be meaningful if it is consistent with other information and if the two points cover a broad enough range of the water quality characteristic. If a meaningful slope is not obtained for any species, go to step B13.

3. Calculate the mean slope (S) as the geometric mean of all of the meaningful slopes for individual species.

4. For each species calculate the geometric mean (T) of the toxicity values (adjusted when necessary) and the geometric mean (C) of the related water quality characteristic values.

5. For each species calculate a value for L, the logarithmic intercept, using the equation: $L=\ln T-S(\ln C)$.

6. Calculate the average logarithmic intercept (I) as the arithmetic average of all of the logarithmic intercepts (L) for individual species.

7. Select the appropriate value for the species sensitivity factor (F):

	Fish		Invertebrates	
	Acute	Chronic	Acute	Chronic
Fresh water...	1.9	6.7	21	5.1
Salt water...	3.7	6.7	49	5.1

8. Calculate J=I/F.

9. For each species calculate the geometric mean (W) of the toxicity values (adjusted when necessary) that were based on measured concentrations and obtained using flow-through procedures and the geometric mean (X) of the related water quality characteristic values.

10. For each species, calculate a value for Y using the equation: $Y=\ln W-S(\ln X)$.

11. Obtain R by selecting the lower of J from step B8 and all the values of Y from step B10.

12. Write the final value as: $e^{[R+S(\ln \text{Water Quality Characteristic})]}$ where the value of R is that obtained in step B11, and the vaule of S is that obtained in step B3.

13. If steps B1–B12 have been completed for fish acute values, invertebrate acute values, fish chronic values, and invertebrate chronic values, go to step C. If not, go to step B1.

C. If, after reviewing all the data, an overall relationship cannot be established between toxicity and any water quality characteristic, go to Section VIII.

D. If a relationship was derived for at least one, but not all, of the four kinds of toxicity data (fish acute, invertebrate acute, fish chronic, and invertebrate chronic), the other relationships should be derived as per steps B4–B12 except that the slope should be obtained by extrapolation from the slopes for the available relationships, rather than as per B3.

E. Go to Section XII.

Section VIII. Final fish acute value

A. For each fish species for which acute values are available calculate the geometric mean of all the acute values (adjusted when necessary).

B. Calculate the geometric mean of all of the geometric means for individual species.

C. Obtain the Final Fish Acute Value by selecting the lower value obtained from 1 and 2:

1. Divide the overall geometric mean by the species sensitivity factor of 3.9 for freshwater fish or 3.7 for saltwater fish (d).

2. For each species calculate the geometric mean of all of the acute values (adjusted when necessary) based on measured concentrations and obtained using flow-through procedures comparable to those in Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975, EPA-660/3-75-009). More than one geometric mean should be calculated for a species if the available information indicates that substantially different acute values are obtained under different test conditions or with different life stages. Select the lowest of all of the means for individual species.

Section IX. Final invertebrate acute value

A. For each invertebrate species for which acute values are available calculate the geometric mean of all the acute values (adjusted when necessary).

B. Calculate the geometric mean of all of the geometric means for individual species.

C. Obtain the Final Invertebrate Acute Value by selecting the lower value obtained from 1 and 2:

1. Divide the overall geometric mean by the species sensitivity factor of 21 for freshwater invertebrates or 49 for saltwater invertebrates (j).

2. For each species calculate the geometric mean of all of the acute values (adjusted when necessary) based on measured concentrations and obtained using flow-through procedures comparable to those in Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians (1975, EPA-660/3-75-009). More than one geometric mean should be calculated for a species if the available information indicates that substantially different acute values are obtained under different test conditions or with different life stages. Select the lowest of all of the means for individual species.

Section X. Final fish chronic value

A. For each fish species for which chronic values are available calculate the geometric mean of all the chronic values.

B. Calculate the geometric mean of all of the geometric means for individual species.

C. Obtain the Final Fish Chronic Value by selecting the lower value obtained from 1, 2 and 3:

1. Divide the overall geometric mean by the species sensitivity factor of 6.7(f).

2. For each species calculate the geometric mean of all of the chronic values. Select the lowest of all of the means for individual species.

3. a. For each matched pair of MATC limits and 96-hr LC50 values from flow-through tests and obtained using measured concentrations, calculate an application factor by dividing the geometric mean of the MATC limits by the 96-hr LC50.

b. Calculate the geometric mean of all of the AF values.

c. Obtain a calculated chronic value from $X\sqrt{YZ}$, where (g)

X=geometric mean AF
Y=geometric mean of the LC50 values used in calculation of X
Z=Final Fish Acute Value from Section VIII.C.

Section XI. Final invertebrate chronic value

A. For each invertebrate species for which chronic values are available calculate the geometric mean of all the chronic values.

B. Calculate the geometric mean of all of the geometric means for individual species.

C. Obtain the Final Invertebrate Chronic Value by selecting the lower value obtained from 1 and 2:

1. Divide the overall geometric mean by the species sensitivity factor of 5.1(k).

2. For each species calculate the geometric mean of all of the chronic values. Select the lowest of all of the means for individual species.

Section XII. Final plant value

A. A plant value can be obtained from a toxicity test on algae, duckweed or other aquatic plant.

B. If no values are available for plants, no Final Plant Value can be derived.

C. Select the lowest plant value as the Final Plant Value.

Section XIII. Residue limited toxicant concentration (RLTC)

A. The RLTC is derived in order to protect (1) wildlife, including fish and birds, that eat aquatic organisms, and (2) the marketability of fish and shellfish. The diets of a variety of wildlife species consist almost entirely of aquatic life and wildlife usually eat the whole body. The marketability of fish and shellfish is determined by FDA action levels.

B. Use (1) an FDA action level or (2) a maximum dietary intake derived from a chronic animal study as a maximum permissible tissue concentration. To obtain a maximum dietary intake, use chronic studies on wildlife if available. Otherwise, use chronic studies on laboratory or domestic animals, such as mice, rabbits, and chickens, when available.

C. If no maximum permissible tissue concentration is available, no RLTC can be derived.

D. Discard each bioconcentration factor (BCF) that is not either (1) a steady-state value or (2) based on an exposure that lasted for 28 days or more. Use a BCF from field exposure only when enough measurements were made of the exposure concentrations. Discard bioconcentration factors obtained from exposures that caused an observable adverse effect on the test organisms. Bioconcentration factors should be corrected for the concentration in the control organisms and should be calculated using wet tissue weights. To convert values expressed on a dry weight basis to wet weight, multiply the dry weight value by 0.1 for plankton and by 0.2 for fish and other invertebrates (1).

E. For use with the result of a chronic animal study, use only BCF values based on whole body measurements on aquatic plants and animals. Calculate the geometric mean for each species, and then the geometric mean of all of the geometric means for individual species.

F. For use with an FDA action level for fish and shellfish, use only BCF values based on muscle (with or without skin) for fish and decapods, adductor muscle for scallops, and total living tissue for other bivalve molluscs. Calculate the geometric mean for each species, and select the highest mean.

G. For use with an FDA action level for animal feed, use only BCF values based on whole body measurements on fish. Calculate the geometric mean for each species, and select the highest mean.

H. For organic chemicals, if no BCF is available for aquatic organisms, a BCF can be obtained (m) from $\text{Log(BCF)} = 0.76 \text{ Log P} - 0.23$, where P is the octanol-water partition coefficient and can be either measured directly or obtained from the retention time on a calibrated reverse phase liquid chromatography system (n). As a last resort, an empirically derived partition coefficient can be used (o). A BCF obtained in this manner applies to aquatic organisms that contain about 8 percent lipids. If it is known that the diet of the wildlife of concern or that the organisms subject to an FDA action level contain a significantly different lipid content, an appropriate adjustment in the estimated BCF should be made.

I. Obtain the RLTC by selecting the lowest value obtained from 1, 2, and 3:

1. Divide the lowest maximum permissible tissue concentration based on a chronic animal study by the BCF obtained in step E or in step H if necessary.

2. Divide the FDA action level for fish and shellfish by the BCF obtained in step F or in step H if necessary.

3. Divide the FDA action level for animal feed by the BCF obtained in step G or in step H if necessary.

Section XIV. Other data

A. For some substances acceptable pertinent information that cannot be used in other sections will be available concerning adverse effects on aquatic organisms and their uses.

B. For some substances data on other obviously important adverse effects, such as flavor impairment or avoidance, may be available.

C. Sometimes LC50 or EC50 values for durations longer than those specified in Sections III and IV for a sensitive species may be lower than the Final Chronic Value, if chronic values are only available for insensitive species.

D. Data from behavioral, microcosm, field, and physiological studies may be available.

Section XV. Final values

A. The Final Acute Value is obtained from the Final Fish Acute Value and the Final Invertebrate Acute Value by selecting the lower available value, or, if toxicity is related to a water quality characteristic, by selecting the value that results in the lower concentrations in the normal range of the water quality characteristic.

B. The Final Chronic Value is obtained from the Final Fish Chronic Value, the Final Invertebrate Chronic Value, the Final Plant Value, and the RLTC by selecting the lowest available value, unless other data (see Section XIV) exist to show that a lower value should be used, or, if toxicity is related to a water quality characteristic, by selecting the value that results in the lowest concentrations in the normal range of the water quality characteristic.

Section XVI. Criterion

A. No criterion can be derived using the Guidelines unless either a Final Fish Chronic Value is available from Section VII or Section X, or a Final Invertebrate Chronic Value is available from Section VII or Section XI, or a good substitute is available from Section XIV for either the final fish or final invertebrate chronic value.

B. The criterion consists of two concentrations, one that should not be exceeded on the average in a 24-hour period and one that should not be exceeded at any time during the 24-hour period. This twofold criterion describes ambient water quality conditions necessary to protect aquatic life and its uses from acute and chronic adverse effects of both cumulative and non-cumulative substances without being as restrictive as a single-number criterion would have to be to provide the same degree of protection.

C. Obtain the 24-hour average concentration by selecting the lower value obtained from 1 and 2:

1. The Final Chronic Value from Section XV.B.

2. 0.44 times the Final Acute Value (q) from Section XV.A.

D. The criterion is the 24-hour average and the concentration should not exceed the Final Acute Value at any time.

Section XVII. Review

A. On the basis of the data collected in Section II and other pertinent information, determine if the criterion is consistent with sound scientific evidence. If it is not, another criterion should be derived using appropriate modifications in the Guidelines. The Guidelines should be modified on a case-by-case basis only if sound scientific evidence indicates the need to do so.

FOOTNOTES

a. The value of 0.77 is the geometric mean of values from 89 tests on 39 toxicants (see Table 1).

b. The value of 0.66, 0.81, and 0.92 are geometric means of 307, 196, and 103 comparisons of 24-, 48-, and 72-hr LC50 values, respectively, with 96-hr LC50 values for fish (see Table 2).

c. The value of 0.71 is the geometric mean of values for 24 pairs of tests on 12 toxicants (see Table 3).

d. The value of 3.9 is the antilog of the product of 1.645 times the square root of the average of the logarithmic variances calculated from 62 sets of fish LC50 values (see Table 4). The value of 1.645 is the t-value for P=0.05 for a one-tailed test so that 95% of the distribution will be above the lower limit. The value of 3.7 is derived similarly for saltwater fish.

e. The value of one-half is used since in only 5 of 75 comparisons were the results of a life cycle test more than a factor of two lower than the results of a comparable embryo-larval test. See: Macek, K. J. and B. H. Sleight, III, 1977. In *Aquatic Toxicology and Hazard Evaluation*, ASTM STP 634, F. L. Mayer and J. L. Hamelink, eds. American Society for Testing and Materials, Philadelphia, PA. pp. 137-146. McKim, J. M., 1977. Jour. Fish Res. Bd. Canada, 34:1148-1154. Hansen, D., Personal Communication, Environmental Research Laboratory, Sabine Island, Gulf Breeze, Florida.

f. The value of 6.7 is the antilog of the product of 1.645 times the square root of the average of the logarithmic variances calculated from 14 sets of freshwater fish chronic values (see Table 5). No comparable data are available for saltwater fish, but 6.7 is probably reasonable since the available chronic values for saltwater fish are, in the same range as those for freshwater fish.

g. See: Andrew, R. W., et al., Evaluation of an Application Factor Hypothesis, Manuscript.

h. The values of 0.26, 0.43, and 0.61 are geometric means of 400, 238, and 29 comparisons of 24-, 48-, and 72-hr LC50 values, respectively, with 96-hr LC50 values for invertebrates (see Table 6).

i. The value of 1.1 is the geometric mean of values for 12 pairs of tests on 8 toxicants (see Table 7).

j. The value of 21 is the antilog of the product of 1.645 times the square root of the average of the logarithmic variances calculated from 25 sets of acute values for freshwater invertebrates (see Table 8). The value of 49 is derived similarly for saltwater invertebrates.

k. The value of 5.1 is the antilog of the product of 1.645 times the square root of the average of the logarithmic variances calculated from 9 sets freshwater invertebrate chronic values (see Table 9). No comparable data are available for saltwater invertebrates, but 5.1 is probably reasonable since the available chronic values for saltwater invertebrates are in the same range as those for freshwater invertebrates.

l. The values of 0.2 and 0.1 were derived from data published in: McDiffett, W. F., 1970. Ecology 51:975-988. Brocksen, R. W., *et al.*, 1968. J. Wildlife Management 32:51-75. Cummins, K. W., *et al.*, 1973. Ecology 54:336-345. Pesticide Analytical Manual, Volume I, Food and Drug Administration, 1969. Love, R. M., 1957. In the Physiology of Fishes, Vol. I, M. E. Brown, ed. Academic Press, New York. p. 411. Ruttner, F., 1963. Fundamentals of Limnology. 3rd ed. Trans. by D. G. Frey and F. E. J. Fry. Univ. of Toronto Press, Toronto. Some additional values can be found in: Sculthorpe, C. D., 1967. The Biology of Aquatic Vascular Plants. Arnold Publishing Ltd., London.

m. Veith, G. D., *et al.* An Evaluation of Using Partition Coefficients and Water Solubility to Estimate Bioconcentration Factors for Organic Chemicals in Fish. (Manuscript.)

n. Veith, G. D., and T. T. Morris, 1978. A Rapid Method for Estimating Log P for Organic Chemicals. Ecological Research Report. EPA-600/3-78-049. U.S. Environmental Protection Agency. Duluth, MN. 15 pp.

o. Leo, A. J., 1975. In *Symposium on Structure-Activity Correlations in Studies of Toxicity and Bioconcentration with Aquatic Organisms.* G. D. Veith and D. E. Konasewich, eds. International Joint Commission, Windsor, Ontario, pp. 151-176.

p. Tests with copper, zinc, diazinon, simzaine, TFM and 2,4-D have shown that exposures to some concentrations above the MATC for short periods of time do not adversely affect survival, growth or reproduction.

q. The value of 0.44 is the geometric mean of the quotients of the highest concentration that killed 0-10% of the organisms divided by the LC50 in 219 acute toxicity tests (see Table 10).

Appendix B-1—Procedures for Obtaining a Criterion When the Guidelines Do Not Produce a Criterion

February 15, 1979.

Alternative procedures were used to derive aquatic life criteria for many of the pollutants for which certain values required by the Guidelines for criterion formulation were not available. The alternative procedures do not replace the Guidelines but supplement them by providing data, estimated values, or assumpations about the subject pollutants so that the Guidelines can be used.

The four alternative procedures developed for this purpose are described briefly below. The procedures are listed in order of preference, that is, the second alternative procedure was considered only if a criterion could not be derived using the first procedure, and so on.

It should be noted that these procedures will not produce a criterion for all chemicals for which the Guidelines will not produce a criterion.

1. Use unpublished data not yet in manuscript form and use the Guidelines to obtain a criterion.

2. A. Assume that, if the 24-hour average concentration is based on 0.44 times the Final Acute Value for a chemical, the same procedure can be used for that chemical for both freshwater and saltwater organisms and for structurally similar organic compounds. (Note: Structurally similar organic compounds are organic chemicals that have the same carbon-oxygen-nitrogen structure and the same arrangement of single, double, and triple bonds, and differ only in the substitution of hydrogen, chlorine, and bromine for each other.)

B. Estimate missing Final Fish Acute Values and Final Invertebrate Acute Values, by assuming that the ratio of the Final Fish Acute Value to the Final Invertebrate Acute Value is the same for a chemical for both freshwater and saltwater organisms and for structurally similar organic compounds.

C. Use the Guidelines to obtain a criterion.

3. A. Assume that, if the 24-hour average concentration is based on the Final Fish Chronic Value for a chemical, the same procedure can be used for that chemical for both freshwater and saltwater organisms and for structurally similar organic compounds.

B. If an actual, not an estimated, Final Fish Acute Value is available, estimate a Final Fish Chronic Value by assuming that either (1) the application factor or (2) the ratio of the Final Fish Chronic Value to the Final Fish Acute Value is the same for a chemical for both freshwater and saltwater organisms and for structurally similar organic compounds.

C. Use the Guidelines to obtain a criterion.

4. If, using the Guidelines, a criterion can be derived for a chemical in one water but not the other, set a criterion for the second water to be equal to that for the first water if (a) data exist to indicate that the toxicity of the chemical to comparable organisms is about the same in both waters, and (b) none of the values necessary to derive the criterion in the first water have to be estimated by procedures other than those described in the Guidelines.

Appendix C—Guidelines and Methodology Used in the Preparation of Health Effect Assessment Chapters of the Consent Decree Water Criteria Documents

I. Objective

The objective of the health effect assessment chapters of the water criteria documents is to estimate ambient water concentrations which protect public health. The assessments review all relevant information on individual chemicals or chemical classes in order to derive criteria which represent, in the case of suspect or proven carcinogens, various levels of incremental cancer risk, and; in the case of other pollutants, "no observable effect levels."

Ideally, water quality criteria should represent levels for compounds in ambient water which would not pose a hazard to the human population. However, in any realistic assessment of human health hazard, a fundamental distinction must be made between absolute safety and recognition of some risk. Criteria for absolute safety would have to be based on detail knowledge of dose/response relationships in humans including all sources of chemi-

cal exposure, the types of toxic effects elicited, the existence of thresholds for the toxic effects, the significance of toxicant interactions, and the variances of sensitivities and exposure levels within the human population. In practice, such absolute criteria cannot be established because of deficiencies in both the available information and the means of interpreting this information. Consequently, the water quality human health effects documents propose criteria which minimize or specify the potential risk of adverse human effects due to substances in ambient water. Potential social or economic costs and benefits are not considered in the formulation of the criteria.

II. TYPES OF CRITERIA

Two types of biological endpoints have been used in developing water quality criteria, stochastic (non-threshold) effects and non-stochastic (threshold) effects.

As defined by the International Commission on Radiological Protection (1977), "*stochastic effects* are those for which the probability of an effect occurring, rather than its severity, is regarded as a function of the dose without threshold." For such effects, which may be regarded as "all or none" phenomena, thresholds or "no effect" levels cannot be established because even extremely small doses must be assumed to elicit a finite increase in the incidence of the response. Carcinogens, mutagens, and, in some cases, teratogens elicit stochastic effects. Consequently, "safe" levels—i.e., levels which will produce no adverse effects—cannot be established for carcinogens and mutagens. Instead, water quality criteria for such compounds are presented as a range of water concentrations associated with a corresponding change in incremental risk.

In contrast, "*non-stochastic effects* are those for which the severity of the effect varies with the dose, and for which thresholds may, therefore, occur." The threshold assumption is based on the premise that in such systems a reserve capacity exists which is thought to be depleted before clinical disease ensues. Since this reserve capacity varies between individuals, it is necessary to incorporate "safety factors" to compensate for possible errors in the derivation of the criterion. Alternatively, it may be assumed that the rate of damage will not be significant over the life span of the organism. Thus, for chemicals which induce only non-stochastic effects, water quality criteria can be derived which will presumably correspond to a "no observable effects level."

In some instances, criteria are based on organoleptic characteristics, i.e., thresholds for taste or odor. Such criteria are established when insufficient information is available on toxicologic effects or when the criterion based on organoleptic effects is below that of the criterion based on toxicologic data. It is recognized that criteria based on organoleptic effects do not necessarily represent satisfactory approximations of low risk levels.

The list of Consent Decree pollutants contains both individual chemical species and classes of compounds. The health assessment chapters, likewise, review information either on broad chemical classes or on individual species as appropriate.

In some cases separate criteria for each chemical in a class are derived because at times even relatively small structural changes can significantly affect chronic toxicity. However, for some chemical classes insufficient data are available on all of the individual compounds of the class. In such instances, a criterion is derived for the entire class or criteria are derived only for certain individual chemicals in the class. The specific reasons for accepting either alternative are detailed in the appropriate health effects chapters.

Lastly, for some chemicals and chemical classes, the data are insufficient for the derivation of any criteria. In these cases, no criteria are given and deficiencies in the available information are detailed.

III. APPROACH

The human health effects chapters attempt to assess all information on the individual chemicals or classes of chemicals which might be useful in developing water quality criteria. Although primary emphasis is placed on identifying epidemiologic and toxicologic data, the assessments typically contain discussions on four topics: Existing levels of human exposure, pharmacokinetics, toxicity, and criterion formulations.

For all documents, an attempt is made to include the known relevant information. Due to severe time constraints, however, an exhaustive literature review was not conducted for 15 documents (Chlordane, Chloroform, Heptachlor, Tetrachloroethylene, Arsenic, Carbon Tetrachloride, Dichloroethylenes, Hexachlorobutadiene, Selenium, Dioxin, Trichloroethylene, Benzene, Beryllium, Dichlorobenzene, Nitrosamines) and these documents were not subjected to formal peer review. For the remaining 50 documents, more detailed literature searches and reviews were performed. Since each of the latter 50 documents was prepared by a scientist who had either conducted original research on the compound or who had previously reviewed the toxicity of the compound, the probability of overlooking significant data is reduced. Review articles and reports were used for data evaluation and synthesis. Scientific judgment was exercised in reviewing and evaluating the data in each document and identifying the adverse effects for which protective criteria are sought. In addition, each of these documents was reviewed by a peer committee of scientists familiar with the compound(s) under consideration. Each committee evaluated the quality of the available data, the completeness of the data summary, and the validity of the derived criterion.

In the analysis and organization of the data, an attempt is made to be consistent in both format and the application of accepted—or at least acceptable—scientific principles. The evaluation procedures used in the hazard assessment process follow the principles detailed by the National Academy of Sciences (1977) in *Drinking Water and Health* and guidelines of the EPA's Carcinogenicity Assessment Group.

Exposure

The exposure section of the health effects chapters reviews known information on the current levels of human exposure to the individual pollutant from all sources. Much of the data were obtained from monitoring studies of air, water, food, soil, and human or animal tissue residues. The major purpose of this section is to provide background information on the contribution of exposure from water relative to all other sources. Consequently, this section is subdivided into exposure from ingestion in water, ingestion in food, inhalation, and dermal contact.

Information with regard to exposure is often valuable in developing a water quality criterion. Typically, a uniform exposure assumption is used in formulating the criteria which includes the consumption of contaminated drinking water and contaminated fish products. Exposure data, however, are useful for comparing the assumed intake to the expected contribution based upon available information. In addition knowledge of exposure from all sources, not limited to drinking water and ingesting fish, can be used to justify the formulation of criteria based upon exposure to ambient water but recognizing contributions to total body intake from additional exposure routes.

The use of fish consumption as a typical exposure factor requires the quantification of pollutant residues in the edible portion of the ingested species. Bioconcentration factors are used to relate the expected pollutant residue in aquatic organisms to the pollutant concentration in the ambient waters in which they live.

In order to estimate the average per capita intake of a pollutant due to consumption of contaminated fish and shellfish, a BCF appropriate for the average U.S. diet was developed. The consumable fish and shellfish were divided into four categories: freshwater fishes, saltwater fishes, molluscs, and decaods (Cordle, et al. 1978). Three different procedures were used for estimating the BCF depending upon the availability of edible portion bioconcentration data and the lipid solubility properties of the chemical. Generally speaking available BCF data are data for the whole fish rather than the edible portions and the data, at best, cover several species.

For lipid-soluble chemicals the average edible portion % lipids is derived for each of the four categories of consumable fish and shellfish products (Sidwell, et al. 1974). Based on consumption factors (Cordle, et al. 1978), the average % lipids are weighted to give the % lipids for the average diet.

Since data indicate that the BCF for lipid-soluble compounds are proportional to the % lipids, factors for whole fish can be adjusted to edible portion BCF's. This is a necessary adjustment since most experimental BCF data are for whole body and not edible portion. Given a specific lipid-soluble pollutant there are, in many cases, at least one BCF and corresponding % lipid value.

With values for the % lipids in the average diet, and the whole fish BCF with corresponding lipid value, a single BCF can be calculated that estimates the weighted average bioconcentration factor.

Example:
Weighted average % lipids for average diet=2.3%
Measured BCF of 17 for trichloroethylene with bluegills at 1% lipids
Weighted average BCF for average diet equals

$$\frac{17\times 2.3\%}{1\%}=39.1$$

As an estimator, 39 is used for the BCF.

In those cases where a measured steady-state bioconcentration factor is not available, the equation "Log BCF=0.76 Log P−0.23" can be used (Veith, et al. 1978) to estimate the BCF for aquatic organisms that contain about 8% lipids from the octanol-water partition coefficient P. An adjustment for % lipids in the average diet versus 8% is made in order to derive the weighted average bioconcentration factor.

For non-lipid-soluble compounds, measured BCF's are needed in order to calculate representative BCF's for each of the four categories of consumed fish and shellfish. Usually, however, BCF information does not exist for all four categories and relative approximations are made based upon known species data. The known and estimated BCF's for each category of fish/shellfish are weighted according to fish consumption factors, and a weighted BCF representative of the average diet is derived.

Example—Given a BCF of 15 for arsenic in bay scallops and other information as shown:

	Average diet consumption (pct)	BCF (estimate)
Freshwater fishes	12	1
Saltwater fishes	61	1
Saltwater molluscs	9	15
Saltwater decapods	18	1

The weighted BCF for arsenic is 2.26 for the average diet. As an estimator, 2.3 is used.

In addition to estimating current levels of human exposure, the exposure section provides, when available, information on special groups at risk based on unusual susceptibility or unusual levels of exposure.

Pharmacokinetics

This section is intended to briefly summarize the available information on the absorption, distribution, metabolism, and elimination of the compound(s) in humans and experimental mammals. Such information can be extremely useful in species to species extrapolation, in assessing the body burdens from long-term low-level exposures, and in characterizing the mode of toxic action. Differences or similarities in pharmacokinetic data on chemicals within a class were sometimes used in evaluating the appropriateness of developing a single water quality criterion for a class of chemicals.

Effects

This section summarizes the following types of information on both humans and experimental mammals:

Acute, subacute, and chronic toxicity
Synergistic or antagonistic (action)
Teratogenicity
Mutagenicity
Carcinogenicity

The major goals of this section are to assess the suitability of the data for use in establishing water quality criteria and to determine which biological endpoint, i.e., stochastic, non-stochastic, or organoleptic, should be selected for use in criterion formulation.

Because this section attempts to assess potential human health effects, data on documented human effects were actively sought. However, several problems with human epidemiological studies usually preclude the use of such data in generating water quality criteria. These problems, as summarized by the National Academy of Science (1977) are presented below:

1. Epidemiology cannot tell what effects a material will have until after humans have been exposed. One must not conduct what might be hazardous experiments on man.
2. If exposure has been ubiquitous, it may be impossible to assess the effects of a material, because there is no unexposed control group. Statistics of morbidity obtained before use of a new material can sometimes be useful, but when latent periods are variable and times of introduction and removal of materials overlap, historical data on chronic effects are usually unsatisfactory.
3. It is usually difficult to determine doses in human exposures.
4. Usually, it is hard to identify small changes in common effects, which may nonetheless be important if the population is large.
5. Interactions in a "nature-designed" experiment usually cannot be controlled.

Although these problems often prevent the use of epidemiological data in quantitative risk estimates, qualitative similarities or differences between documented effects in humans and observed effects in experimental mammals are extremely useful in assessing the validity of animal-to-man extrapolations. Therefore, in each case an attempt is made to identify and utilize both epidemiologic and animal dose reponse data. Criteria derived from such a confirmed data base are considered to be most reliable.

The decision to establish a criterion based on stochastic effects is made by evaluating information on carcinogenicity and mutagenicity. The first steps in the process of estimating risk are to determine whether the compound is likely to cause cancer in humans and to determine whether the data are adequate for the derivation of a water quality criterion. The criteria for the qualitative decision of carcinogenicity are outlined briefly in the EPA Interim Cancer Guidelines (May, 1976), in an article by Albert, et al. (1977), and in the IRLG guidelines on carcinogenic risks (IRLG, 1979). The assumption is made that a substance which induces a statistically significant response in animals by any route of exposure has the capability of causing cancer in humans from ingestion of this substance in water and edible aquatic organisms taken from that water. A chemical which has not induced a significant cancer response in humans or experimental animals is not identified as a possible carcinogen, even though its metabolites or close structural analogues might induce a carcinogenic response or even though they are mutagenic in *in vitro* systems.

It is recognized that some potential human carcinogens would not be identified by the rules above. However the derivation of a criterion concentration cannot be justified for them. There are other compounds for which there

is plausible, but weak, qualitative evidence of carcinogenicity in experimental animal systems but which cannot be given a valid criterion concentration. This occurs in cases where the only evidence of animal or human carcinogenicity is obtained in a special carcinogen bioassay system such as mouse skin painting or strain A mouse pulmonary adenoma. The derivation of a criterion concentration for human consumption from these studies is considered invalid regardless of the qualitative outcome. In addition there are some compounds (e.g., nickel and beryllium) which are carcinogenic in humans via inhalation in one chemical form but have induced no response in animals or humans via ingestion of their soluble salts. For beryllium a criterion concentration is developed because of a finding of tumors in animals at a site removed from the injection site, but for nickel no criterion is recommended because no evidence of tumors exists from administration of nickel solutions by either ingestion or injection.

For those compounds which were not reported to induce carcinogenic effects or for those compounds on which carcinogenic effects data were lacking or insufficient, an attempt is made to define a "No Observable Effect Level (NOEL)". In many respects, the evaluation of these studies is similar to that of carcinogenicity bioassays. In order to more closely approximate conditions of human exposure, preference is given to chronic studies involving oral exposures (dietary or in water) over a significant proportion of the organisms life span. Greatest confidence is placed in those studies which demonstrated dose related adverse effects as well as no effect levels. Considerable variability was encountered in the biological endpoints used to define NOELs which ranged from gross effects such as mortality to more subtle changes in biochemical, physiological, or pathological parameters. Given the variety of effects which some chemicals cause and the problems encountered in animal-to-man extrapolations, the derivation of a NOEL was obtained using chronic data if available. Teratogenicity, reproductive impairment, and behavioral effects may be significant consequences of environmental contamination. However, when such effects were seen, carcinogenic or other chronic toxic effects were usually also observed and subsequently used in deriving the criterion. Teratogenicity studies, for the most part, involve doses near the maximum tolerated levels and administration schedules which do not reasonably approximate environmental exposures. Studies designed to determine reproductive impairment are often conducted over long periods at low doses. However, the threshold doses for reproductive effects often exceed the threshold for other biological endpoints (e.g., changes in organ weights). Information on behavioral effects, which is of considerable potential significance, is not available on most of the compounds under study. Consequently, most NOEL's derived from chronic studies are based either on gross toxic effects or on effects which can be directly related to functional impairment or defined pathological lesions.

For compounds on which adequate chronic toxicity studies are not available, studies on acute and subacute toxicity assume greater significance. Acute toxicity studies usually involve single exposures at lethal or near lethal doses. Subacute studies usually involve exposures over about 10% of the life span of the test organisms, e.g., 90 days for the rat with an average life span of 30 months. Such studies are useful in establishing the nature of the toxic effects, including the target organs, metabolic behavior, physiological/biochemical effects, and patterns of retention and tissue distribution. The utility of acute and subacute studies in deriving environmentally meaningful NOEL's is uncertain although McNamara (1976) has developed application factors for such derivations.

In some cases where adequate data are not available from studies using oral routes of administration, NOEL's for oral exposures are estimated from dermal or inhalation studies. Such estimates involved approximations of the total dose based on assumptions about breathing rates and/or magnitude of absorption.

Criterion rationale

This section reviews existing standards for the chemical(s), summarizes data on current levels of human exposure, attempts to identify special groups at risk, and defines the basis for the recommended criterion.

Information on existing standards is included primarily for comparison with the proposed water quality criteria. Some of these standards, such as those recommended by Occupational Safety and Health Administration (OSHA) or American Conference of Governmental Industrial Hygienists (ACGIH), are based on toxicological data but are intended as acceptable levels of occupational rather than environmental exposure. Other levels, such as those recommended by the National Academy of Sciences (1977) in *Drinking Water and Health* or in the EPA *Interim Primary Drinking Water Standards* are more comparable to the proposed water quality criteria. Emphasis is placed on detailing the bases for the existing standards, wherever possible.

Summaries of current levels of human exposure presented in this section specifically address the applicability of the data to generating water quality criteria. The identification of special groups at risk—either because of geographical or occupational differences in exposure or biological differences in susceptibility to the compound(s) focused on the impact that these groups should have on the development of water quality criteria.

In the section on the basis for the recommended criteria all of the data used in developing the criteria were summarized and, if necessary, qualified.

IV. GUIDELINES FOR CRITERIA DERIVATION

The derivation of water quality criteria from data on laboratory animal toxicity tests is essentially a two step procedure. First, a total daily intake for humans must be estimated which establishes either a defined level of risk for stochastic effects or NOEL for non-stochastic effects. Secondly, some assumptions must be made about the contribution of contaminated water and fish/shellfish consumption to the total daily intake of the chemical. These assumptions may then be used to calculate the water quality criterion as it relates to the tolerable daily intake.

A. Stochastic Effects

After the decision has been made that the compound has the potential of causing cancer in humans and that data exist which permit the development of a criterion, the water concentration which is estimated to cause a lifetime carcinogenic risk of 10^{-6} is determined. This concentration is calculated by fitting the available data to a dose-response model. A risk level of 10^{-6} was selected for the purpose of comparing the carcinogenic effects among the various compounds. The model chosen for this purpose incorporates several concepts assembled from different sources. The basic dose response model is the "one-hit" model.

$$(1)\ P=1-\exp[-BD]$$

where P is the probability of getting an observable case of cancer in a lifetime because of exposure to a daily dose D of the compound, and B is a constant determined by the data. The quantity B is the only parameter in the model and it is interpreted as a quantitative indicator of the carcinogenic effectiveness of the compound. At low doses (low enough so that $P<0.1$), P is directly proportional to the dose D and B is the slope of the dose-response line obtained when P is plotted against D. Because the model approximates a straight line through the origin at low doses, it is sometimes called a linear, no-threshold dose-re-

sponse model. It states that any exposure to a carcinogen, however small, results in some chance of cancer occurrence, and the probability (or the risk) of getting cancer from low exposure increases linearly with the dose.

This model is used for risk estimations because it is consistent with three basic concepts in chemical carcinogenesis: (a) The dose-response curve for mutagenesis in bacterial systems is linear with no threshold for both radiation- and chemical-induced damage; (b) there are both theoretical reasons, based on valid concepts of the mechanisms of chemical carcinogenesis, as well as a wealth of data, which indicate that chemicals which cause mutations are likely to induce cancer in animals and therefore presumably in people; and (c) epidemiology studies in human populations exposed to animal carcinogens (radiation, aflatoxin, cigarette smoke) show an incidence-exposure relationship that is linear down to very small doses with no evidence of a threshold.

Evidence for some chemicals suggests that extremely small doses are "detoxified" safely and therefore do not contribute to the induction of cancer. If this were true the risk at such low exposures would be either zero or much smaller than the one-hit model would predict. The possibility of threshold mechanisms has given support to other dose-response models (Guess, et al. 1977) for extrapolation of cancer risk such as the log-probit, logit and multi-stage models. These models are non-linear and result in lower risks than the one-hit model for a given low exposure.

Since the experimental tumor incidence data generally provide no clue as to which model is correct, the choice must be made on the basis of policy. The agency has chosen the one-hit model because it is consistent with the three basic facts previously mentioned and because it gives greater risk estimates than other plausible models. The entire procedure, both in the choice of the model and in the selection of which of several sets of carcinogenic data to use in the model, is designed to determine roughly how severe the carcinogenic hazard could be if the chemical does have the potential of causing cancer in humans. The hazard is not likely to be higher but could be lower if some threshold or non-linear response exists. Therefore the water quality criterion concentrations derived from the procedure are intended to be estimates of the smallest concentrations that are likely to give rise to a 10^{-5} risk.

In analyzing animal data where the control (untreated) group has a spontaneous incidence of tumors equal to P_c and the treated group has an incidence of the same tumor type of P_t, the incidence that can be attributed to the treatment alone, P, can be found by the following argument. If the process initiating a spontaneous tumor is independent of the chemical process which initiates an induced tumor, then in the treated group where both processes are occurring simultaneously, the animals have tumors either because they are spontaneous (with probability P_c) or because they are not spontaneous (which has probability $1-P_c$) and they are induced by the chemical (with a probability P). Therefore

(2) $P_t=P_c+(1-P_c)P$ and $P=(P_t-P_c)/(1-P_c)$

The quantity P, due to chemically-induced tumors, is the quantity appearing in the one-hit model, equation (1). The correction for spontaneous tumors given in equation (2) is called the Abbott's correction. Using it, the one-hit model takes the form:

(3) $P=(P_t-P_c)/(1-P_c)=1-\exp[-BD]$

Another modification of the one-hit model is needed to deal with experiments that are terminated earlier than the natural lifetime of the animals because of early tumor occurrence and for cases where the data are given in terms of the time when a certain fraction (usually 50%) of the animals have tumors. It is known, from an extensive series of rat experiments by Druckrey (1967) with different nitrosamine compounds, that for a certain daily dosage, d, the time when 50% of the animals get tumors, t_{50} is shorter with higher doses and the relationship between t_{50} and d is $d(t_{50})^m=K$, where K and m are constants characteristic of the compound. He found that for the compounds tested m ranged from 2.0 to 4.0 with most of them close to 3.0. This observation is consistent with the findings of Doll (1971) that the age progression of human chemically-induced cancers also increases as t^3. This time dependence of the progression of tumors during a lifetime can be incorporated into the one-hit model for lifetime incidence (equation 3) by expressing time as fraction of a lifetime and writing

(4) $P=(P_t-P_c)/(1-P_c)=1-\exp[-BDt^3]$

This formulation of the dose-response model is equivalent to equation (3) for lifetime exposures. If the chemical is so potent and the doses are so large that treated animals die prematurely at times significantly less than 1.0, then the premature termination of the experiment will have the effect of increasing the value of B, the potency of the compound.

The dose-response model (4) has features of the Weibull time-to-tumor model (Peto, 1973), which is $P=k(t-w)^m$, where w, k and m are constants. This can be shown by noticing that, for small doses D, equation (4) is approximately $P=Bdt^3$ which is the Weibull model with m=3, w=0 and k=Bd.

Selection of data and use of the extrapolation model

After determining that a substance is carcinogenic and that the existing information is adequate for developing a water criterion, a choice must be made of which of the data sets from several studies to use in the model. For some chemicals, several studies in different animals species and strains, each run at several doses and possible different routes of exposure, are available. It is also necessary to correct for metabolism differences between species and absorption factors via different routes. The procedures used in evaluating these data are consistent with the approach of making a maximum-likely risk estimate.

They are listed below:

(1) The tumor incidence data are separated according to the organ site or tumor type. For each dose group the tumor incidence in treated versus controls is tested for significance using the Fisher exact test at the $p<0.05$ level of significance.

(2) The set of data (i.e., the dose and incidence data) used in the model is the set where the incidence is statistically significantly higher than controls at the lowest dose group. If the lowest dose group has more than one tumor site that is statistically significant, then the set used is the one which given the highest value of the potency factor B. In case both matched and pooled controls are reported (as in the NCI bioassay program), the pooled controls are not used if their tumor incidence is significantly different from matched controls. When the two control groups are not significantly different, the one giving the highest value of B is actually used, although in this case the choice of controls usually has only a trivial effect on the value of B.

(3) Each of the available carcinogenicity reports is analyzed in a similar way. The dose units in each report are converted to mg/kg/day averaged over the time span of the study (the time until terminal sacrifice).

In calculating the mg/kg/day equivalent of a dietary dose of a certain ppm, a standard conversion factor (F), assumed to be characteristic of the species, is used as follows: mg/kg/day=ppm×F. The factor F is the percent of the adult animal weight that is consumed as food each day. For rats, F=0.05; for mice, F=0.13. For comparison of inhalation and ingestion experiments, the assumption is made that 100% is absorbed via each route

unless experimental measurements are available.

(4) The value of B used for the criterion is the highest value obtained from any of the studies.

(5) Dose conversions between species are done on a body surface area basis. It is known that the effective dose, d, in mg per day of direct-acting drugs is proportional to the body surface area. This relationship holds for humans of various sizes from infants to adults and for extrapolations between laboratory animals and humans. It is known to be approximately true also for oxygen and calorie consumption rates. Since a crude approximation to body surface area is the body weight, w, to the (⅔)rds power, one can write $d=k/(w)^{⅓}$, so that the ratio between the animal specific dose, $(d/w)_A$, and the equivalent human specific dose, $(d/w)_H$ is:

$$\frac{(d/w)_H}{(d/w)_A} = \left(\frac{w_A}{w_H}\right)^{1/3}$$

Therefore the specific dose (mg/kg/day) to humans required to produce an effect is smaller than the specific dose that would produce that effect in animals. It follows that, when the doses are expressed as mg/kg body weight/day, the potency in humans is higher than that in animals by the ratio $(W_H/W_A)^{⅓}$.

(6) If human epidemiology studies and associated exposure information are available for the compound they are always used in some way. If they show a carcinogenic effect, even when the route is inhalation, the data are analyzed to give an estimate of the linear dependence of cancer rates on lifetime average dose, which is equivalent to the factor B. If they show no carcinogenic effect then it is assumed that the real value of B is less than can be observed in the experiment, and an upper limit value of B is calculated assuming hypothetically that the true incidence is just below the level of detection in the cohort studied, which is determined largely by the sample sizes. Whenever possible human data are used in preference to animal bioassay data.

Calculation of the water quality criterion concentration

After the value of B has been determined the lifetime risk, P, from an average daily exposure of ×mg/kg/day is found from the equation P=B×. Therefore if the lifetime risk is set at $P=10^{-5}$ for calculation purposes, the intake, I, in mg/day for a 70-kg person can be found by the equation:

(5) $I=70\times10^{-5}/B$.

The exposure to ambient water is assumed to come from two sources: (a) drinking an average of 2 litters of water per day, and (b) ingesting an average of 18.7 grams of fish per day (Cordle, 1978). Because of accumulation of residues in fish, the amount of the pollutant in fish (mg/kg of edible fish) is equal to a factor R times the water concentation (mg/kg of water). Therefore the total intake I can be written as the sum of two terms:

I(mg/day)=C(mg/l)×R(l/kg fish)×0.0187 kg fish/day
+ C(mg/l)×2 l/day
=C(0.0187 × R×2),

Where C is the water concentration in mg/l. Therefore the water concentration can be found from equation (5) as follows:

(6) $C=70\times10^{-5}/B(2+R\times0.0187)$

This is the equation for calculating the water quality criterion for a pollutant. Under certain circumstances, criteria for exposure conditions other than 2 liters of water/day and 18.7 gms fish/day may be desired. Lifetime risk levels other than 10^{-5} may also be of interest. In such circumstances equation (7) is used and the desired levels substituted as follows:

$$(7)\quad C = \frac{70 \times (\text{lifetime risk level})}{B[(\text{Water intake}) + R \times (\text{Fish intake})]}$$

For example a criterion level for a lifetime risk of 10^{-6} at an exposure of 50 grams of fish/day and 1 l/day of water is

$$C = \frac{70 \times 10^{-6}}{B \quad (1 + R \times 0.050)}$$

The interpretation of these equations is that if the lifetime average water concentration is kept lower than the calculated value, the lifetime risk is estimated to be lower than 10^{-5}. If a low dose threshold could be reliably established for the compound the risk would be lower than 10^{-5}.

The following is a summary of slope factors which can be used for calculating criteria for exposure risk levels other than those presented in the assessment documents. Note that in cases where human data are available a model different from the one-hit model is used for dose-response calculation. For these cases an equivalent slope factor is derived. Also included is a summary for a criterion based on a 10^{-5} lifetime risk assuming lifetime daily consumption of 2 liters of water and 0.0187 kg fish.

Chemical	Slope factor, B (mg/l/day)$^{-1}$	Example of toxicant concentration corresponding to a risk level of 10^{-5} (μg/l)
Arsenic	14.00 *	0.029
Benzene	0.02160 *	0.15
Cadmium	1.09658 *	0.28
Chloroform	0.14695	2.1
Beryllium	3.4308	0.087
Carbon Tetrachloride	0.090996	2.6
Chlordane	5.36196	1.2×10^{-3}
1,1-Dichloroethylene	0.25292*	1.3
Heptachlor	30.3063	0.23×10^{-3}
Hexachlorobutadiene	0.04949	0.77
Dimethylnitrosamine	13.4	0.026
Diethylnitrosamine	38.2	0.0092
Dibutylnitrosamine	26.86	0.013
N-Nitroso-pyrrolidine	3.297	0.11
Tetrachlorodioxin	13.923	4.6×10^{-7}
Tetrachloroethylene	0.08440	2.0
Trichloroethylene	0.01200	21
Vinyl Chloride	0.00066*	520

Mathematical description of extrapolation method

1. *Information from Chronic Study*

nt=Number of animals exposed to the selected dose that developed tumors at some time in the study. See text for explanation of selection criteria for choosing the data set.
NT=Total number of animals exposed to selected dose level.
nc=Number of control animals with tumors.
NC=Total number of control animals.
Le=Actual maximum lifespan for test animals.
le=Length of exposure.
d=Average dose per unit of time (mg/kg/day) during administration of the agent.
w=Average weight of test animals (kg).

2. *Information from general literature*

70 kg=Average weight of people.
L=Theoretical average length of life for test species, unless specified in article. It is 90 weeks for mice and 104 weeks for rats.
F=Average weight of fish consumed per day, assumed 0.0187 kilograms.

3. *Other information*

R=Bioconcentration factor for edible portions of fish (Supplied by Environmental Research Laboratory, Duluth).

4. *Mathematical Model*

$Pt=Pc+(1-Pc)\times[1-e^{-t_{MD}}]$

where

Pt=nt−NT=Proportion of test animals with tumors.

Pc=nc−NC=Proportion of control animals with tumors.

$$D = \frac{d \times le}{Le} = \text{Lifespan weighted average dose level mg/kg/(unit of time).}$$

$$B_A = -\ln\left[\frac{1 - Pt}{1 - Pc}\right] \div [D \times t^3]$$

where $t = \frac{\text{lifespan for test animals}}{\text{length of life for species}} = \frac{Le}{L}$

$$B_H = B^3\sqrt{\frac{70}{w}}$$

$$C = \frac{70 \times 10^{-5}}{B_H(2+RxF)} = \text{criterion level (mg/l) for man.}$$

B. Non-Stochastic Effects

A somewhat less formalized approach is used in the derivation of water quality criteria based on non-stochastic effects. As previously described, an attempt is made to identify studies defining NOEL's in mammals. For many compounds, several effect and no effect levels are reported in the literature. The NOEL's selected for deriving the criteria is the highest NOEL that did not exceed a level reported to cause adverse effect.

The NOEL is transformed into an Acceptable Daily Intake for man (ADI) by dividing by an uncertainty factor of 10, 100, or 1,000. The guidelines for using the uncertainty factors, as given by the National Academy of Sciences (1977), are outlined below:

1. Valid experimental results from studies on prolonged ingestion by man, with no indication of carcinogenicity.

Uncertainty Factor=10

2. Experimental results of studies of human ingestion not available or scanty (e.g., acute exposure only). Valid results of long-term feeding studies on experimental animals or in the absence of human studies, valid animal studies on one or more species. No indication of carcinogenicity.

Uncertainty Factor=100

3. No long-term or acute human data. Scanty results on experimental animals. No indication of carcinogenicity.

Uncertainty Factor=1,000

For a few of the chemicals or chemical classes, ADIs are estimated from threshold limit values (TLVs) or subacute/acute mammalian data. TLV's are established by the ACGIH and represent estimated levels of the compounds in the work environment which are not anticipated to result in significant adverse health effects in workers exposed 8 Hours/day, 5 days/week. The method used to derive ADIs from TLVs is essentially that recommended by Stokinger and Woodward (1958) and is based on assumptions of the breathing rate and completeness of absorption.

Once an ADI is established, assumptions are made concerning the relative contribution of water to total human exposure. In some cases, criteria are developed in a manner analogous to that used in carcinogenicity studies:

$$C=ADI/2+0.0187\times R$$

In other cases, the bioconcentration term is omitted and an approximation is made of the proportion of the exposure attributed to water and non-water sources. For all compounds, criteria is based on an assumed daily water consumption of 2 liters.

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APPENDIX D—SUMMARY OF COMMENTS CONCERNING GUIDELINES FOR DERIVING WATER QUALITY CRITERIA FOR THE PROTECTION OF AQUATIC LIFE

On May 18, 1978, the Agency published for comment a methodology for developing water quality criteria (43 FR 21506) for the protection of aquatic life and its uses, and invited public comment on all aspects of the methodology.

Following is a brief review of the comments the Agency has received regarding the methodology. Fifty-eight comments were received from interested parties including private industry, consultants, environmental groups, State governments, and other Federal agencies.

I. ISSUES CONCERNING THE PURPOSE, INTENT, AND APPLICATION OF THE METHODOLOGY

Many commenters thought that the criteria should account for differing water characteristics. Others stated that there is a need to develop a systematic means for interpreting data and for estimation of effects where data are unavailable. Additional comments were received regarding the similarity of guideline results with "Red Book" results, the use of existing data versus development of new data, concern that the criteria may be lower than ambient levels, and that the scientific community should be involved in the development of the guidelines.

II. ISSUES REGARDING STANDARDIZATION OF ACUTE TOXICITY DATA

Many respondents commented on the procedure for standardizing the acute toxicity data. Principal issues that were raised were the effect of multiple correction factors on predic-

tion error, data variability, the use of mean values as correction factors, the scientific justification for standardizing acute toxicity data, the rationale used for rejections of data, the assumptions used regarding log-normal data distributions, the sufficiency of the data base for the correction factors, and the need for subgroupings for correction factors.

III. ISSUES CONCERNING STANDARDIZATION OF CHRONIC DATA VALUES

The principal comments the Agency received regarding the standardization of chronic data were the use of geometric mean for data correction factor, the adequacy of existing MATC data, and the range of variation of data used for standardization.

IV. ISSUES CONCERNING THE DERIVATION OF FINAL LC50 AND MATC VALUES

The Agency received many comments concerning the derivation of final LC50 and MATC values. The most frequent comments regarded the variation of species response to individual toxicants, the effect of the variation of toxicant physical and chemical property variation, the variability of individual toxicants within a given species, the selection of the lowest LC50 value as a final acute value, and the adequacy of the chronic test data base for marine species. Additional comments were received on the differing methods used for determining LC50's, the limited data base for determining MATC confidence intervals, the variation of application factors, and the justification for calculated chronic values (X YZ).

V. ISSUES CONCERNING THE PLANT EFFECTS PROCEDURES AND VALUES

The comments the Agency received regarding plant effects, procedures and values concerned the adequacy of the existing data base, the selection of the lowest plant value, and the interpretation of plant value guidelines.

VI. ISSUES CONCERNING BIOCONCENTRATION EFFECTS PROCEDURES AND VALUES

The principal issues raised by commenters concerning bioconcentration effects concerned the use of the Octanol/H O partition coefficient, the appropriateness of using FDA action levels, the validity of oral dose data, the basis for determination of bioconcentration factors, and the justification of metabolic and biomagnification factors.

VII. ISSUES CONCERNING DERIVATION OF TWO-FOLD CRITERION

The issues raise by commenters concerning the derivation of two-fold criterion pertained to the acceptability of 96-hour final acute time period, the adequacy of safety margins, the soundness of rationale for two-fold criterion, the degree of protection provided by procedures for developing criteria, application factor variation, the economic feasibility of monitoring standards, and the chronic data base.

VIII. OTHER ASPECTS OF THE GUIDELINES DATA BASE

Other aspects of the guidelines data base which were commented on concerned the use of field data on actual water body conditions where possible, the screening of data for reliability, and the completeness of data usage.

IX. ISSUES CONCERNING THE PRESENTATION AND DOCUMENTATION OF THE GUIDELINES

Many respondents commented on the presentation and documentation of the guidelines. The principal comments concerned clarification of the guidelines instructions and procedures, the need for definition of terms used in the guidelines, the use of nonpublished data, and the adequacy of tables used in the guidelines.

X. OTHER ISSUES NOT INCLUDED UNDER ANY OF THE ABOVE

Miscellaneous issues raised by respondents and not mentioned above are that the Agency failed to consider certain classes of organisms, the guidelines methodology should be field-tested, there should be a continual updating of "correction" and "sensitivity" factors, more attention should be given to the influence of water quality on toxicity, the recognition of differences between field and laboratory bioassay conditions, the differences between the dissolved fraction and total concentration of toxicant, and the toxicant mode of action.

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